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CHEMOTHERAPY OF RODENT MALARIA

ANNUAL REPORT

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A technique is described in this report for the evaluation of drug interactions with combinations containing only one active antimalarial agent. The relative merits of chloroquine-resistant strains of P.berghei and P.yoelii ssp. as laboratory models of P.falciparum are discussed.

Blood schizontocidal action of 8 WRAIR compounds and 1 compound from another source is summarised. Data from cross-resistance studies on 29 different sensitive and resistant strains are included. In a series of drug interaction tests to determine the influence of 4 WRAIR compounds on the action of chloroquine against chloroquine-resistant P.yoelii ssp. NS strain, only WR 014044 enhanced the activity of chloroquine. A high degree of synergism was demonstrated with a combination of two different isomers of the floxacrine analog WR 243251.

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FOREWORD

In conducting research using animals, the investigator(s) adhered to the "Guide for the Care and Use of Laboratory Animals" prepared by the Committee on Care and Use of Laboratory Animals of the Institute of Laboratory Animal Resources, National Research Council (NIH Publication No. 86-23, Revised 1985).

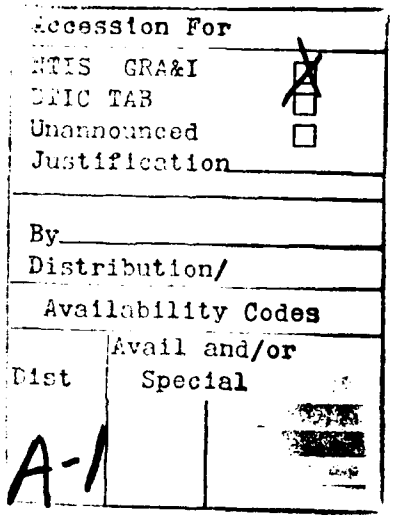


TABLE OF CONTENTS

	Page
Report Documentation Page	
Foreword	1
1. INTRODUCTION	3
2. ADMINISTRATIVE EVENTS	3
3. CHEMOTHERAPY STUDIES	4
3.1 Evaluation of data from drug interaction studies.	4
3.2 The role of chloroquine resistant strains of rodent malaria in experimental chemotherapy.	6
3.3 Blood schizontocidal activity.	9
3.4 Cross resistance studies.	11
3.5 Drug interaction studies.	11
4. PUBLICATIONS	13
APPENDIX 1 Summary of blood schizontocidal activity tests	14
APPENDIX 2 Cross-resistance studies	33
APPENDIX 3 Drug interaction studies	117

1. INTRODUCTION

In the period since that covered in the last Annual Report, eight new compounds have been submitted for testing by WRAIR. These have been examined for blood schizontocidal activity and, in some instances, the compounds have also been studied in drug interaction experiments.

The problems which we had experienced with cytoplasmic polyhedrosis virus in the mosquito colony have been largely overcome by a continuing programme of treatment of the stock cages. Transmission of malaria through the mosquitoes is better now than at any time since the colony was established.

A reassessment of the comparative usefulness of chloroquine resistant strains of *Plasmodium berghei* and *P.yoelii* as models for *P.falciparum* has led us to revise our method of calculating resistance indices (I_{90}), and a new way of demonstrating quantitatively the degree of interaction between two drugs, where one compound has no antimalarial activity in its own right, has been developed.

2. ADMINISTRATIVE EVENTS.

Staff employed on US Army funds are as follows:

Senior Technologist/ Research Assistant	- B.L.Robinson	100% Time
Techicians	- Ms A.West	100% Time
	- Ms J.R.Cox	100% Time
Secretary	- Mrs B.A.Sargeaunt	25% Time

Mrs Sargeaunt has recently retired, and the part time secretarial post has not yet been filled.

Other staff associated with the project but not financially supported by USAMRDC are:

Professor W.Peters (Principal Investigator)	20% Time

Dr D.C.Warhurst (Biologist) 20% Time

Dr S.L.Croft (Electron Microscopist) 10% Time

3. CHEMOTHERAPY STUDIES

3.1 Evaluation of data from drug interaction studies

Until recently, our studies on drug interactions have been involved with pairs of compounds, each of which possess significant degrees of antimalarial activity in their own right. Determining the effect of compounds like these upon one another could be done easily by constructing isobolograms, which illustrated graphically the presence of synergism or antagonism.

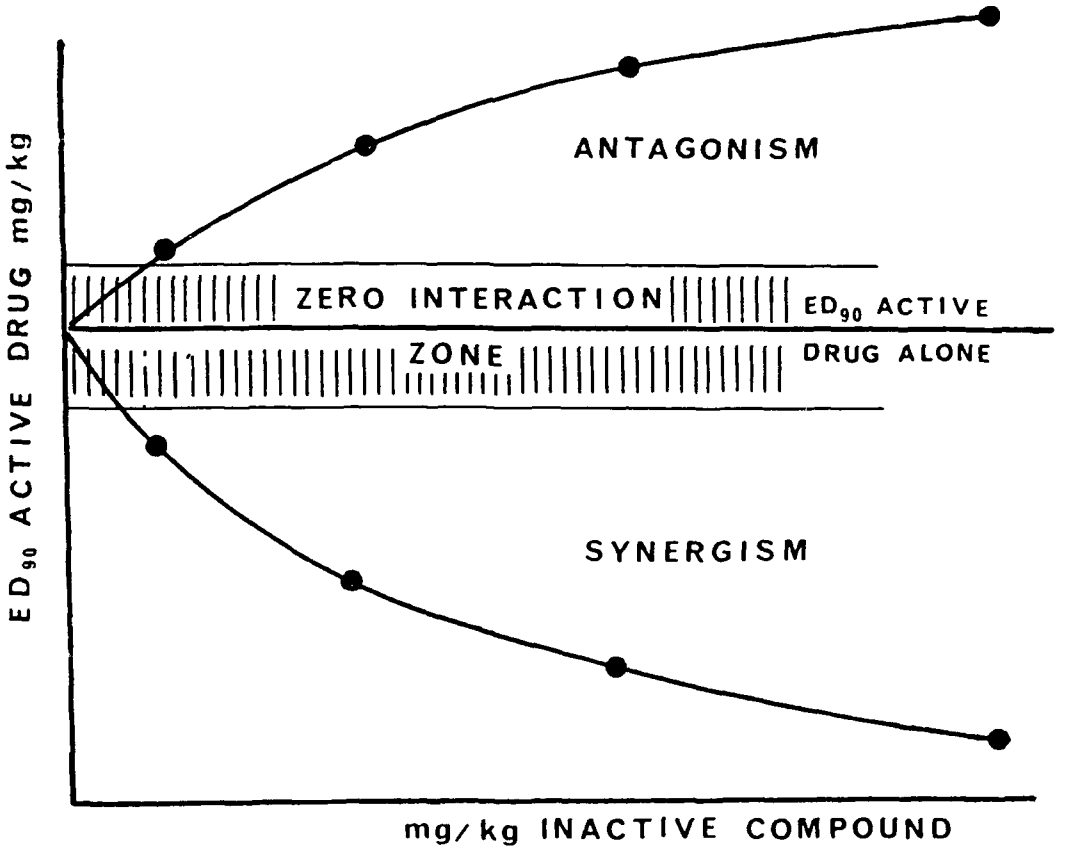
It has, however, becoming increasingly the case that interest in using compounds such as calcium channel blockers, which have little or no inherent antimalarial activity, to influence the action of chloroquine on chloroquine resistant parasites has provided us with pairs of compounds in which only one drug has a direct antimalarial effect. Clearly, this prevents the construction of a conventional isobologram for use in analysing the interaction between the two compounds, since the presence or absence of synergism can only be demonstrated by this technique when the ED_{90} of each of the pair is known.

To overcome this problem we have devised a method to illustrate graphically and to quantify the influence of an antimalarially inactive compound, eg Verapamil, on the activity of a known antimalarial, eg chloroquine, in our rodent model.

Graphically, this is done by plotting the ED_{90} of the active partner against varying dosage of the antimalarially inert drug on a simple graph which also has a line indicating

the ED_{90} of the active drug drawn onto it. Figure 1 illustrates this principle and shows how the different types of interaction present themselves by this technique. The single compound ED_{90} line may be bounded by the extreme limits of confidence and points falling within this zone are indicative of a total failure to influence the activity of the antimalarial partner. Synergism is demonstrated by a graph which drops away from the ED_{90} line toward the bottom axis, whilst if antagonism is present between the two compounds the curve will rise progressively as the dose increases.

Figure 1. Graphic illustration of drug interactions where only one of the paired drugs possesses innate antimalarial activity.



A quantitative assessment of the degree of influence

of inactive compound on its antimalarial partner is made by calculating the Activity Enhancement Index (AEI). This involves a simple calculation in which the ED_{90} of the active compound alone is divided by the ED_{90} of the paired drugs at each dose of the "inert" compound.

For example, in order to directly compare the influence of a second compound on the efficacy of chloroquine, we compare the ED_{90} of chloroquine alone (CQ) with that of chloroquine combined with the test compound (CQ + "Drug X") i.e.

$$AEI = \frac{CQ}{CQ + \text{"Drug X"}}$$

In effect, this regards the activity of chloroquine alone as representing an AEI of 1.0 and enhanced activity resulting from the combination of chloroquine with a second compound produces an AEI value greater than 1.0. This will apply whether the companion compound possesses antimalarial activity in its own right or not, and regardless of the cause of enhancement e.g. synergism or reversal of resistance. Similarly, an antagonistic interaction would lead to the AEI being reduced to a value lower than 1.0.

The use of AEI analysis not only permits a direct comparison to be made between a series of compounds in separate experiments, but may also be used to indicate the dose of an individual compound which produces optimal enhancement of activity.

3.2 <u>The role of chloroquine resistant strains of rodent malaria in experimental chemotherapy.</u>

Our preliminary studies on the effect of calcium channel blockers, which used Verapamil as a representative

compound, were carried out on the highly chloroquine-resistant RC strain of P. berghei. No evidence of any activity was detected with Verapamil, neither alone nor in combination with chloroquine. However, when these experiments were repeated using P.yoelii ssp. NS strain, marked potentiation of the effect of chloroquine was noted, although Verapamil alone still produced no reduction at all in the parasitaemia. This phenomenon was also experienced with other Verapamil derivatives which were examined by us in our role as a World Health Organisation Reference Centre.

We have long felt that P.yoelii NS is a better model for chloroquine resistant P.falciparum than P.berghei RC (see Peters et al., 1975, Ann.trop.Med.Parasitol., 69:155 - 171), and when these experiments were repeated using NS strain, marked enhancement of the activity of chloroquine occurred with most of the Verapamil derivatives. These results, which are compatible with those previously obtained with Verapamil itself used in combination with chloroquine in vitro against chloroquine resistant strains of P.falciparum, help to confirm the value of the NS strain as a suitable in vivo model for P.falciparum.

When these observations are considered in conjunction with the data obtained in our cross resistance studies, it becomes clear that not only is P.yoelii ssp. NS strain a superior in vivo model to P.berghei RC for P.falciparum but that, for the purposes of studies on blood schizontocidal activity and resistance, direct comparisons should not normally be made between P.berghei N strain and the NS strain. This constraint also applies to resistant lines derived from these two distinct species.

Table 1. A comparison of blood schizontocidal activity of a range of antimalarial compounds against P.berghei N strain and P.yoelii ssp NS strain. ED90 values are expressed in mg/kg X 4 sc.

COMPOUND	ED_{90} N STRAIN	ED_{90} NS STRAIN
CHLOROQUINE	3.1	56.0
AMODIAQUINE	2.6	18.0
PRIMAQUINE	4.8	8.4
MEPACRINE	4.6	18.3
QUININE HCl (po)	118.0	290.0
CINCHONINE HCl (po)	125.0	220.0
QUINIDINE HCl (po)	31.0	195.0
MEFLOQUINE HCl (po)	4.6	7.2
HALOFANTRINE	1.1	1.0
ARTEMISININ	4.2	10.0
PYRONARIDINE	0.7	1.2
PYRIMETHAMINE (ip)	0.12	0.13
SULFADOXINE	4.4	0.26
FANSIDAR *	0.32	0.1
CYCLOGUANIL	3.3	6.9
MENOCTONE	1.4	4.5
FLOXACRINE	1.0	0.6
CLINDAMYCIN	36.0	55.0
DOXYCYCLINE	2.7	98.0

* PYRIMETHAMINE : SULFADOXINE (1:3)

It is apparent from Table 1 that the normal response of the NS strain to a substantial number of antimalarial drugs differs significantly from that of P.berghei N strain. These inherent differences also influence the resistance patterns of strains resistant to specific compounds which may be developed from these and, therefore, the response of any of these derived strains should only be assessed against the appropriate parent strain. For example, the ED_{90} of chloroquine against the mefloquine-resistant NS1100 strain is 27.0 mg/kg. If this is compared with that of the N strain (3.1 mg/kg ; I_{90} = 1.0) then one would say that an almost ninefold resistance to chloroquine has developed in the course of producing mefloquine resistance (I_{90} = 8.8). However, when the comparison is drawn with the parent NS

strain, which has an ED_{90} of 56.0 mg/kg, it is immediately apparent that in fact approximately half of the resistance to chloroquine possessed by the parent strain was lost in the process of producing the mefloquine resistance (I_{90} NS1100 = 0.5). This same principle applies to any drug tested against resistant lines.

We have accordingly altered our previous practice of comparing all strains employed in blood schizontocidal activity tests with N strain to derive resistance factors, and in this and future reports we will be making comparisons with the appropriate parent strain. Summary sheets will therefore show two series of data for each compound in order to give as accurate a picture as possible of patterns of resistance.

3.3 Blood schizontocidal activity studies

Results from the blood schizontocidal activity tests are summarised in Tables 3 to 5, and detailed test data are contained in Tables 6 through 20.

(i) BK73252 and BL47346 (WR numbers not known)

These two compounds were tested for activity against P.berghei N strain, N1100, Q, KFY (resistant to mefloquine, quinine and Fansidar respectively), the chloroquine resistant P.yoelii ssp. NS and the artemisinin resistant ART (derived from NS).

BK73252 was the more active of the two compounds with an ED_{90} in N strain of 0.08 mg/kg X 4 sc. Slight resistance to this compound was observed in the Q and KFY strains (I_{90} values : 2.5 and 2.4), but since this compound is tolerated at doses in excess of 100 mg/kg the therapeutic index is probably still very good. The NS was only slightly less

sensitive (ED_{90} : 0.15 mg/kg) and the ART showed a level of resistance comparable with the Q and KFY.

BL47346 was appreciably less active (ED_{90} N strain: 7.9 and NS: 9.0 mg/kg). The other resistant lines, apart from KFY, showed some resistance, ranging from an I_{90} value of 2.3 in the N1100 to 4.6 in the ART strain. The KFY strain was slightly more sensitive than the parent N strain (I_{90}: 0.7).

(ii) Floxacrine analogues

Three floxacrine analogues have been received for testing. The first, WR 243251, has a similar level of activity to floxacrine against N strain (ED_{90}: 1.5 mg/kg X 4 sc). No cross resistance was observed in the N1100, Q and KFY strains of P.berghei, or in P.yoelii ssp. NS and ART.

The other two analogues were isomers of WR 243251. The R-isomer (WR 250547) was much less active with an ED_{90} of 83.0 mg/kg in N strain, but the L-isomer (WR 250548) had a level of activity through all the strains comparable to that of WR 243251.

(iii) Fusidic acid)

This compound was tested for blood schizontocidal activity prior to investigating its potential use in controlling cytoplasmic polyhedrosis virus in our mosquito colony. Slight antimalarial activity was detected against N strain (ED_{90}: >300 mg/kg X 4 sc).

(iv) Nifedipine (WR 255695 AE) and Diltiazem (WR 255693 AC)

These two calcium antagonists had been identified by workers at WRAIR as having an enhancing effect on the activity of chloroquine against P.falciparum in vitro. Prior to investigating this aspect in vivo, both compounds were tested for inherent antimalarial activity. Nifedipine was inactive at 100 mg/kg and Diltiazem hydrochloride showed only

very slight activity (ED_{90}: 540 mg/kg) against the N strain but was inactive against P.yoelii ssp. NS at 100 mg/kg X 4 sc.

(v) Phenytoin (WR 014044)

This compound was also submitted in connection with combination studies, although the hypothesis advanced was that simultaneous treatment with phenytoin and chloroquine would result in antagonism between the two compounds. Some blood schizontocidal activity was detected when phenytoin was tested against the N strain (ED_{90}: 150 mg/kg).

3.4 Cross-resistance studies

Our extended studies of the cross-resistance patterns of twenty-nine different sensitive and resistant strains of rodent malaria subjected to treatment with a range of twenty-one antimalarials is now nearing completion. Data from blood schizontocidal activity tests are included as Tables 25 to 103 and complete results of the cross-resistance studies completed to date are given in Tables 21 to 24.

3.5 Drug interaction studies

3.5.1 WR 014044 and chloroquine

As a result of the clinical failure of chloroquine in the treatment of P.faiciparum in some patients receiving phenytoin, the hypothesis had been advanced that an interaction occurs between the two compounds effectively enhancing the parasite's resistance to chloroquine. In the in vivo rodent model, using P.yoelii ssp. NS strain, this did not prove to be the case. Indeed, phenytoin possesses some antimalarial activity in its own right and a clearly synergistic interaction was shown when chloroquine was administered simultaneously (Figure 2 and 3).

3.5.2 WR 255695 and chloroquine

Combination therapy with these two compounds (Figure 4) produces no more than a slight enhancement of the activity of chloroquine against the NS strain.

3.5.3 WR 255693 and chloroquine

Simultaneous treatment with Diltiazem hydrochloride aand chloroquine has little more effect than treatment with chloroquine alone in the in vivo drug interaction test (Figure 5).

3.5.4 WR 250547 and WR 250548

A drug interaction test was performed to investigate the possible effects of administering these two isomers of the floxacrine analogue WR 243251 together. A high degree of synergism was obvious with this combination (Figure 6).

Table 2. Activity enhancement analysis of some WRAIR compounds combined with chloroquine. Verapamil data are included for comparison.

LON	BN No.	WRAIR	Dose	ED_{90} CQ	AEI
2109	Verapamil	hydrochloride	-	23.0	-
			1.0	28.0	0.82
			3.0	21.0	1.10
			10.0	12.5	1.84
			30.0	8.0	2.88
2164	BL 51831	014044	-	27.0	-
			1.0	23.0	1.17
			3.0	18.8	1.44
			10.0	14.2	1.90
			30.0	7.6	3.55
2142	BL 48656	255696 AE	-	25.0	-
			3.0	16.0	1.56
			10.0	17.8	1.40
			30.0	17.5	1.43
			60.0	15.5	1.61
2143	BL 19657	255693 AC	-	24.0	-
			3.0	24.0	1.00
			10.0	24.0	1.00
			30.0	23.0	1.04
			60.0	16.5	1.45

4. PUBLICATIONS

BROSSI, A., Venugoplan, B., Dominguez Gerpe, L., Yeh, H.J.C., Flippen-Andersen, J.L., Buchs, P., Luo, X.D., Milhous, M. and Peters, W. (1988) Arteether, a new antimalarial drug: synthesis and antimalarial properties. J.Medicinal Chemistry, 31, 645-650.

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APPENDIX 1

SUMMARY OF BLOOD SCHIZONTOCIDAL ACTIVITY TEST DATA

SUMMARY OF BLOOD SCHIZONTOCIDAL (4 DAY TEST) DATA

	Route	N		N1100		Q		KFY									
		ED 50	ED 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I
LON 2145 WR BK 73252	sc	0.05	0.08	0.07	0.9	0.2	2.5	0.19	2.4								
LON 2146 WR BL 47346	sc	3.9	7.9	18.5	2.3	30.5	3.9	5.7	0.7								
LON 2159 WR 243251 BL 21100	sc	0.4	1.5	1.0	0.7	0.6	0.4	1.4	0.9								
		NS		ART													
		ED_{50}	ED_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I
LON 2145 WR BK 73252	sc	0.07	0.15	0.37	2.5												
LON 2146 WR BL 47346	sc	5.2	9.0	41.0	4.6												
LON 2159 WR 243251 BL 21100	sc	0.5	1.0	1.2	1.2												

Table 3

ED_{50} / ED_{90} = mg/kg x 4 MTD = maximum tolerated dose

SUMMARY OF BLOOD SCHIZONTOCIDAL (4 DAY TEST) DATA

	Route	N		N1100		Q		KFY									
		ED_{50}	ED_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I
LON 2160 WR 250547 BL 29759	SC	10.3	83.0														
LON 2161 WR 250548 BL 34170	SC	0.6	2.0	2.5	1.25	1.1	0.6	1.8	0.9								
LON 2147 Fusidic Acid	SC	100	>300														
		NS		ART													
		ED_{50}	ED_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I
LON 2160 WR 250547 BL 29759	SC	5.7	23.0														
LON 2161 WR 250548 BL 34170	SC	1.2	2.0	1.3	0.7												
	SC																

Table 4

ED_{50} / ED_{90} = mg/kg x 4 MTD = maximum tolerated dose

SUMMARY OF BLOOD SCHIZONTOCIDAL (4 DAY TEST) DATA

	Route	N															
		ED_{50}	ED_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I
LON 2142 WR 255695 AE BL 48656	sc	>100	≫100														
LON 2143 WR 255 693 AC BL 48657	sc	80.0	540														
LON 2164 WR 014044 BL 51831	sc	30.0	150														
		NS															
		ED_{50}	ED_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I
LON 2142 WR 255695 AE BL 48656	sc	>100	≫100														
LON 2143 WR 255693 AC BL 48657	sc	>100	≫100														
	sc																

ED_{50} / ED_{90} = mg/kg x 4 MTD = maximum tolerated dose

Table 5

SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 6

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME WR (Bk 73252)

OR NUMBER LON 2145 PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80/H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ≥100 MG/KG X 4.

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.01	5		-	100 ± 0.6
	0.03	5		-	98.9 ± 4.0
N	0.1	5	1	-	1.0 ± 0.4
	0.3	5		-	0.01 ± 0.01
	1.0	5		-	0
	∅	10		22.6	

ED_{50}(range) 0.05(0.03-0.13)

ED_{90}(range) 0.08(0.04-0.21)

Resistance factor I_{90} 1.0

	0.01	5		-	76.9 ± 10.1
	0.03	5		-	75.1 ± 10.9
N1100	0.1	5	1	-	3.5 ± 0.8
	0.3	5		-	0.03 ± 0.03
	1.0	5		-	0
	∅	10		6.8	

ED_{50}(range) 0.03(0.02-0.05)

ED_{90}(range) 0.07(0.04-0.11)

Resistance factor I_{90} 0.9

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 7

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME WR (BK 73252)

OR NUMBER LON 2145 PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80/H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ≥100 MG/KG X 4

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.01	5		-	71.8 ± 5.7
	0.03	5		-	54.9 ± 6.3
Q	0.1	5	1	-	50.9 ± 11.7
	0.3	5		-	40.9 ± 14.7
	1.0	5		-	0.03 ± 0.01
	Ø	10		6.4	
ED_{50}(range) 0.05(0.01-0.32)					
ED_{90}(range) 0.2(0.05-1.1)					
Resistance factor I_{90} 2.5					
	0.01	5		-	100 ± 0.7
	0.03	5		-	100
KFY	0.1	5	1	-	48.8 ± 18.9
	0.3	5		-	0.5 ± 0.3
	1.0	5		-	0
	Ø	10		16.8	
ED_{50}(range) 0.1(0.07-0.12)					
ED_{90}(range) 0.19(0.13-0.22)					
Resistance factor I_{90} 2.4					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 8

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME WR (BK 73252)

OR NUMBER LON 2145 PARASITE (SUB)SPECIES P.yoelii ssp.

FORMULATION Tween 80/H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ≥100 MG/KG X 4.

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.01	5		-	100 ± 1.5
	0.03	5		-	60.4 ± 6.1
NS	0.1	5	1	-	52.9 ± 3.5
	0.3	5		-	3.4 ± 2.4
	1.0	5		-	0
	Ø	10		21.3	
ED_{50}(range) 0.07 (0.03-0.11)					
ED_{90}(range) 0.15 (0.07-0.25)					
Resistance factor I_{90} 1.0					
	0.01	5		-	100
	0.03	5		-	100
ART	0.1	5	1	-	100
	0.3	5		-	29.8 ± 10.0
	1.0	5		-	0.01 ± 0.01
	Ø	10		23.3	
ED_{50}(range) 0.26 (0.23-0.29)					
ED_{90}(range) 0.37 (0.33-0.4)					
Resistance factor I_{90} 2.5					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 9

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME WR (BL47346)

OR NUMBER LON 2146 PARASITE (SUB)SPECIES P.berghei

FORMULATION Tween 80/H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ≥100. MG/KG X 4.

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	1.0	5		-	100
	3.0	5		-	71.0 ± 7.1
N	10.0	5	1	-	4.4 ± 1.3
	30.0	5		-	0.02 ± 0.01
	Ø	10		22.6	

ED_{50}(range) 3.9 (3.4 – 4.6)

ED_{90}(range) 7.9 (6.8 – 9.5)

Resistance factor I_{90} 1.0

	1.0	5		-	78.4 ± 8.1
	3.0	5		-	59.4 ± 12.1
N1100	10.0	5	1	-	48.8 ± 16.3
	30.0	5		-	5.0 ± 1.4
	Ø	10		6.8	

ED_{50}(range) 3.9 (1.9 – 15.3)

ED_{90}(range) 18.5 (9.0 – 73.0)

Resistance factor I_{90} 2.3

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES) TABLE 10

COMPOUND NAME WR (BL 47346)

OR NUMBER LON 2146 PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80/H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ≥100 MG/KG X 4.

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	1.0	5		–	66.5 ± 8.7
	3.0	5		–	46.8 ± 11.4
Q	10.0	5	1	–	46.2 ± 10.8
	30.0	5		–	5.0 ± 2.7
	Ø	10		6.4	

ED_{50} (range) 3.8 (1.1 – 12.6)

ED_{90} (range) 30.5 (8.5 – 105)

Resistance factor I_{90} 3.9

	1.0	5		–	78.0 ± 9.0
	3.0	5		–	56.5 ± 14.7
KFY	10.0	5	1	–	3.2 ± 1.0
	30.0	5		–	0.01 ± 0.01
	Ø	10		16.8	

ED_{50} (range) 2.2 (1.4 – 4.5)

ED_{90} (range) 5.7 (3.6 – 11.8)

Resistance factor I_{90} 0.7

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE II

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME WR (BL 47346)

OR NUMBER LON 2146 PARASITE (SUB)SPECIES P.yoelii ssp.

FORMULATION Tween 80/H_2O. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) >100. MG/KG X 4.

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	1.0	5		-	96.9 ± 3.1
	3.0	5		-	93.9 ± 3.0
NS	10.0	5	1	-	15.3 ± 4.2
	30.0	5		-	0
	Ø	10		21.3	

ED_{50}(range) 5.2 (1.9 - 6.7)

ED_{90}(range) 9.0 (3.4 - 12.0)

Resistance factor I_{90} 1.0

	1.0	5		-	87.4 ± 8.6
	3.0	5		-	75.3 ± 10.7
ART	10.0	5	1	-	58.2 ± 12.0
	30.0	5		-	14.9 ± 4.2
	Ø	10		23.3	

ED_{50}(range) 7.3 (2.9 - 20.0)

ED_{90}(range) 41.0 (16.0 - 110)

Resistance factor I_{90} 4.6

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 12

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME WR 243251 (BL 21100)

OR NUMBER LON 2159 PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80/H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) >10 MG/KG X 4

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.1	5		-	81.3 ± 4.0
	0.3	5		-	75.3 ± 2.3
N	1.0	5	1	-	20.1 ± 6.6
	3.0	5		-	1.5 ± 0.9
	Ø	10		24.8	

ED_{50}(range)	0.4 (0.2 - 0.7)
ED_{90}(range)	1.5 (0.8 - 2.8)
Resistance factor I_{90}	1.0

	0.1	5		-	100 ± 6.6
	0.3	5		-	80.2 ± 14.4
N 1100	1.0	5	1	-	18.2 ± 6.2
	3.0	5		-	0.04 ± 0.04
	10.0	5		-	0
	Ø	10		4.9	

ED_{50}(range)	0.5 (0.4 - 0.7)
ED_{90}(range)	1.0 (0.7 - 1.4)
Resistance factor I_{90}	0.7

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES) TABLE 13

COMPOUND NAME WR 243251 (BL21100)

OR NUMBER LON 2159 PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80 / H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ≥10 MG/KG X 4

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.1	5		-	100 ± 3.1
	0.3	5		-	76.8 ± 11.5
Q	1.0	5	1	-	0.8 ± 0.5
	3.0	5		-	0
	10.0	5		-	0
	Ø	10		7.3	
ED_{50} (range) 0.4 (0.3-0.5)					
ED_{90} (range) 0.6 (0.5-0.8)					
Resistance factor I_{90} 0.4					
	0.1	5		-	88.4 ± 3.0
	0.3	5		-	87.4 ± 2.4
KFY	1.0	5	1	-	21.4 ± 7.8
	3.0	5		-	1.0 ± 0.2
	10.0	5		-	0.01 ± 0.01
	Ø	10		19.9	
ED_{50} (range) 0.5 (0.4-0.8)					
ED_{90} (range) 1.4 (1.1-2.2)					
Resistance factor I_{90} 0.9					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 14

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME WR 243251 (BL 21100)

OR NUMBER LON 2159 PARASITE (SUB)SPECIES P. yoelii ssp.

FORMULATION Tween 80/H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ≥10 MG/KG X 4.

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.1	5		-	99.7 ± 5.0
	0.3	5		-	90.6 ± 3.7
NS	1.0	5	1	-	1.5 ± 0.4
	3.0	5		-	0.8 ± 0.6
	∅	10		20.2	

ED_{50}(range)	0.5 (0.2-1.0)
ED_{90}(range)	1.0 (0.4-1.9)
Resistance factor I_{90}	1.0

	0.1	5		-	97.5 ± 1.6
	0.3	5		-	91.5 ± 6.7
ART	1.0	5	1	-	1.1 ± 0.2
	3.0	5		-	0.2 ± 0.1
	10.0	5		-	0.08 ± 0.07
	∅	10		19.9	

ED_{50}(range)	0.6 (0.25-1.9)
ED_{90}(range)	1.2 (0.5-3.8)
Resistance factor I_{90}	1.2

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 15

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME WR 250547 BL 29759

OR NUMBER LON 2160 PARASITE (SUB)SPECIES P.berghei

FORMULATION Tween 80 / H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) >10.0 MG/KG X 4.

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.1	5		-	95.5 ± 3.3
	0.3	5		-	89.2 ± 5.8
N	1.0	5	1	-	92.5 ± 3.0
	3.0	5		-	80.0 ± 4.0
	10.0	5		-	52.9 ± 7.1
	Ø	10		24.7	

ED_{50}(range)	10.3(8.0-15.0)
ED_{90}(range)	83.0(65.0-118)
Resistance factor I_{90}	

ED_{50}(range)	
ED_{90}(range)	
Resistance factor I_{90}	

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES) TABLE 16

COMPOUND NAME WR 250547 BL 29759
OR NUMBER LON 2160 PARASITE (SUB)SPECIES P.yoelii ssp.

FORMULATION Tween 80/H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) >10.0 MG/KG X 4

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.1	5		-	93.7 ± 4.5
	0.3	5		-	88.7 ± 5.3
NS	1.0	5	1	-	92.1 ± 2.3
	3.0	5		-	82.7 ± 6.4
	10.0	5		-	22.7 ± 9.3
	Ø	10		26.3	

ED_{50}(range)	5.7(3.0 - 11.0)
ED_{90}(range)	23.0(11.8-43.0)
Resistance factor I_{90}	

ED_{50}(range)	
ED_{90}(range)	
Resistance factor I_{90}	

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 17

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME WR 250548 (BL34170)

OR NUMBER LON 2161 PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80/H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) >10 MG/KG X 4

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.3	5		-	78.0 ± 3.0
	1.0	5		-	65.9 ± 7.3
N	3.0	5	1	-	1.5 ± 0.3
	10.0	5		-	0.17 ± 0.08
	Ø	10		24.8	

ED_{50}(range) 0.6(0.3-1.8)

ED_{90}(range) 2.0(1.1-6.1)

Resistance factor I_{90} 1.0

	0.1	5		-	73.3 ± 12.0
	0.3	5		-	65.6 ± 16.7
N 1100	1.0	5	1	-	43.3 ± 13.2
	3.0	5		-	8.1 ± 2.3
	10.0	5		-	1.7 ± 1.2
	Ø	10		4.9	

ED_{50}(range) 0.4(0.1-1.2)

ED_{90}(range) 2.5(0.8-7.2)

Resistance factor I_{90} 1.25

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 18

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME WR 250548 (BL 34170)

OR NUMBER LON 2161 PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80 / H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ≥10 MG/KG X 4.

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.1	5		-	100
	0.3	5		-	64.3 ± 14.1
Q	1.0	5	1	-	36.8 ± 2.1
	3.0	5		-	0.03 ± 0.03
	10.0	5		-	0
	Ø	10		7.3	
ED_{50}(range) 0.6(0.3-0.9)					
ED_{90}(range) 1.1(0.5-1.6)					
Resistance factor I_{90} 0.6					
	0.1	5		-	100 ± 2.2
	0.3	5		-	88.4 ± 1.6
KFY	1.0	5	1	-	28.3 ± 7.7
	3.0	5		-	5.8 ± 2.7
	10.0	5		-	0.02 ± 0.01
	Ø	10		19.9	
ED_{50}(range) 0.6(0.4-1.0)					
ED_{90}(range) 1.8(1.2-2.8)					
Resistance factor I_{90} 0.9					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 19

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME WR 250548 (BL 34170)

OR NUMBER LON 2161 PARASITE (SUB)SPECIES P.yoelii ssp.

FORMULATION Tween 80/H_2O. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) >10 MG/KG X 4

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.3	5		-	100 ± 1.4
	1.0	5		-	76.9 ± 8.5
NS	3.0	5	1	-	0.4 ± 0.4
	10.0	5		-	0
	Ø	10		20.2	

ED_{50}(range) 1.2(0.6-1.5)

ED_{90}(range) 2.0(1.1-2.5)

Resistance factor I_{90} 1.0

	0.1	5		-	100 ± 0.3
	0.3	5		-	96.0 ± 1.6
ART	1.0	5	1	-	8.9 ± 3.2
	3.0	5		-	0.9 ± 0.2
	10.0	5		-	0.01 ± 0.01
	Ø	10		28.3	

ED_{50}(range) 0.6(0.4-0.9)

ED_{90}(range) 1.3(0.8-1.9)

Resistance factor I_{90} 0.7

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 20

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME Fusidic Acid

OR NUMBER LON 2147 PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80/H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) >300 MG/KG X 4.

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	3.0	5		-	79.7 ± 7.4
	10.0	5		-	68.3 ± 6.5
N	30.0	5	1	-	55.3 ± 8.0
	100.0	5		-	52.6 ± 6.9
	300.0	5		-	47.2 ± 4.4
	Ø	10		19.8	

ED_{50}(range)	100(20-310)
ED_{90}(range)	>300
Resistance factor I_{90}	

ED_{50}(range)	
ED_{90}(range)	
Resistance factor I_{90}	

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

APPENDIX 2

CROSS-RESISTANCE STUDY DATA

	N	RC	Q	N1100	NH	P	B	PYR	ORA	MEN	NPN	N1708	MFY	KFY	PFMA	N1765	NAM	QM
CHLOROQUINE	3.1	230	»60	4.5	7.0	2.3	4.8	3.5	3.6	3.0	25.0	10.2	5.7	3.9	20.0	4.0	270	305
AMODIAQUINE	2.6	420	»30	20.0	5.4	2.0	2.1	3.3	2.6	4.5	32.0	5.2	6.2	2.6	6.2		350	300
WR 228258	10.0	13.0	»100	26.0	»100	0.25	0.47	0.63	0.4	0.91	141	178	1.3	2.4	29.0	97.7	3400	»100
PRIMAQUINE	4.8	13.0	18.5	9.0	10.5	74.0	6.4	24.0	2.6	3.3	8.4	7.0	20.5	10.5	20.5	9.2	45.0	21.0
QUININE	118	1280	»600	1700	210	140	170	130	190	40.0	900	175	180	130	165	310	850	2000
CINCHONINE	125	4700	»600	400	290	85.0	50.0	91.0	63.0	60.0	550	90.0	257	25.4	17500	275	600	»600
QUINIDINE	31.0	92.0	470	305	117	85.0	35.0	93.0	54.0	155	580	88.0	152	71.0	127	100	550	700
MEFLOQUINE	4.6	275	» 60	540	9.0	13.5	6.0	5.6	4.2	2.5	6.8	5.3	10.0	4.0	7.7	4.4	95.0	850
HALOFANTRINE	1.1	»100	»100	135	3.6	1.5	4.2	2.3	1.9	0.7	3.5	1.5	2.0	3.4	2.3	1.1	30.0	>100
MEPACRINE	1.9	17.0	190	195	4.7	2.9	4.6	1.1	2.1	4.8	45.0	12.3	4.8	3.4	16.0	38.0	410	»30
ARTEMISININ	4.2	430	267	17.0	10.5	12.0	8.2	4.8	7.5	6.2	90.0	5.9	9.5	8.8	20.8	13.9	538	52.0
PYRONARIDINE	0.7	10.0	>100	1.6	0.8	1.0	1.4	1.1	1.5	0.7	13.5	0.7	0.9	0.7	1.2	1.3	2.6	9.0
PYRIMETHAMINE	0.12	0.05	0.03	0.04	0.26	0.17	2.4	3.4	0.5	0.4	0.21	0.01	29.6	3.7	0.07	1.2	0.26	0.05
SULFADOXINE	4.4	0.62	0.13	0.04	2.7	0.39	0.71	1.2	29.0	0.34	0.1	1.2	3.7	57.0	<0.3	0.9	<0.3	0.12
FANSIDAR*	0.32	0.06	0.01	0.08	0.16	0.2	0.5	0.6	0.48	0.07	0.03	0.1	38.0	37.0		0.33	0.05	0.05
CYCLOGUANIL	3.3	3.6	3.4	2.5	6.4	320	»100	»100	44.0	5.2	10.0	3.7	1000	70.0	1.9	3.5	26.0	4.0
MENOCTONE	1.4	11.0	1.8	1.2	1.6	2.1	9.0	7.2	2.7	3700	1.8	2.3	1.6	2.5	2.0	1.5	2.0	2.9
FLOXACRINE	1.0	0.27	0.5	0.3	0.8	0.4	0.4	0.4	0.4	1.0	0.3	0.6	0.5	0.45	0.4	0.8	0.7	0.7
CLINDAMYCIN	36.0	56.0	9.7	2.9	57.0	6.4	27.0	6.0	8.8	7.5	9.0	27.0	19.5	28.0	16.5	19.0	18.5	13.8
DOXYCYCLINE	2.7	3.8	9.3	33.0	20.0	3.2	17.5	8.5	180	13.0	9.0	18.5	32.0	5.1	42.0	12.0	11.5	18.0
LON 1765	1.7	8.2	560	34.5	39.0	2.1	3.1	3.2	4.0	5.1	6.6	11.0		4.8		100		

* Pyrimethamine : Sulfadoxine (1:3)

Table 21. ED_{90} values of some antimalarial drugs against resistant lines of P. berghei.

	N	RC	Q	N1100	NH	P	B	PYR	ORA	MEN	NPN	N1708	MFY	KFY	PFMA	N1765	NAM	QM
CHLOROQUINE	1·0	74.2	>19.4	1·5	2·3	0·7	1·5	1·1	1·2	1·0	8·1	3·3	1·8	1·3	6·5	1·3	87·1	98·4
AMODIAQUINE	1·0	162	>11·5	7·7	2·1	0·8	0·8	1·3	1·0	1·7	12·3	2·0	2·4	1·0	2·4		135	115
WR 228258	1·0	1·3	»10	2·6	»10	<0·3	<0·3	<0·3	<0·3	<0·3	14·1	17·8	0·13	<0·3	<0·3	9·8	340	»10
PRIMAQUINE	1·0	2·7	3·9	1·9	2·2	15·4	1·3	5·0	0·5	0·7	1·8	1·5	4·3	2·2	4·3	1·9	9·4	4·4
QUININE	1·0	10·8	»5·0	14·4	1·8	1·2	1·4	1·1	1·6	0·3	7·6	1·5	1·5	1·1	1·4	2·6	7·2	16·9
CINCHONINE	1·0	37·6	»4·8	3·2	2·3	0·7	0·4	0·7	0·5	0·5	4·4	0·7	2·1	0·2	140	2·2	4·8	»4·8
QUINIDINE	1·0	3·0	15·2	9·8	3·8	2·7	1·1	3·0	1·7	5·0	18·7	2·8	4·9	2·3	4·1	3·2	17·7	22·6
MEFLOQUINE	1·0	60.0	»13	117	2·0	2·9	1·3	1·2	0·9	0·5	1·5	1·2	2·2	0·9	1·7	1·0	20·7	185
HALOFANTRINE	1·0	»91	»91	123	3·3	1·4	3·8	2·1	1·7	0·6	3·2	1·4	1·8	3·1	2·1	1·0	27·3	>91
MEPACRINE	1·0	8·9	100	103	2·5	1·5	2·4	0·6	1·1	2·5	23·7	6·5	2·5	1·8	8·4	20·0	>5·3	»15·8
ARTEMISININ	1·0	102	63·5	4·0	2·5	2·9	2·0	1·1	1·8	1·5	21·4	1·4	2·3	2·1	5·0	3·3	128	12·4
PYRONARIDINE	1·0	14·3	»143	2·3	1·1	1·4	2·0	1·6	2·1	1·0	19·3	1·0	1·3	1·0	1·7	1·9	3·7	12·9
PYRIMETHAMINE	1·0	0·4	0·25	0·3	2·2	1·4	20·0	28·3	4·2	3·3	1·8	0·08	247	30·8	0·6	10·0	2·2	0·4
SULFADOXINE	1·0	0·14	0·03	0·01	0·6	0·09	0·16	0·3	6·6	0·08	0·02	0·3	0·8	13·0	<0·07	0·2	<0·07	0·03
FANSIDAR	1·0	0·18	0·03	0·25	0·5	0·6	1·6	1·9	1·5	0·2	0·09	0·3	119	116		1·0	0·16	0·16
CYCLOGUANIL	1·0	1·1	1·0	0·8	1·9	97·0	»30	»30	13·3	1·6	3·0	1·1	303	21·2	0·6	1·1	7·9	1·2
MENOCTONE	1·0	7·9	1·3	0·9	1·1	1·5	6·4	5·1	1·9	2643	1·3	1·6	1·1	1·8	1·4	1·1	1·4	2·1
FLOXACRINE	1·0	0·3	0·5	0·3	0·8	0·4	0·4	0·4	0·4	1·0	0·3	0·6	0·5	0,45	0·4	0·8	0·7	0·7
CLINDAMYCIN	1·0	1·6	0·3	0·1	1·6	0·2	0·8	0·2	0·2	0·2	0·3	0·8	0·5	0·8	0·5	0·5	0·5	0·4
DOXYCYCLINE	1·0	1·4	3·4	12·2	7·4	1·2	6·5	3·1	66·7	4·8	3·3	6·9	11·9	1·9	15·6	4·4	4·3	6·7
LON 1765	1·0	4·8	329	20·3	22·9	1·2	1·8	1·9	2·4	3·0	3·9	6·5		2·8		58·8		

>5·0 Resistant	2·5-5·0 Slightly resistant	0·7-2·5 Sensitive	0·5-0·7 Slightly hypersensitive	<0·5 Hypersensitive

Table 22. Resistance factors (I_{90}) of resistant strains of P. berghei to some antimalarial drugs.

	NS	NS1100	SH	SPN	NS1708	ART	NS1765	SAM	MPS	QMS	NIG
CHLOROQUINE	56·0	27·0	80·0	220	21·5	400	210	520	480	650	6·7
AMODIAQUINE	18·0	4·8	»100	420	31·0	310	78·3	112	510	»100	6·3
WR 228258	2·9	90·0	0·4	156	125	»30	140	>100	»100	145	0·75
PRIMAQUINE	8·4	18·4	9·2	13·7	9·0	11·5	10·2	220	9·5	20·0	19·5
QUININE	290	600	190	920	200	400	270	1080	8500	925	220
CINCHONINE	220	70·0	»600	1600	155	700	253	660	3200	»600	115
QUINIDINE	195	230	1050	1000	72·0	385	115	490	620	5400	115
MEFLOQUINE	7·2	640	»100	20·0	7·5	65·0	11·0	128	180	»100	5·2
HALOFANTRINE	1·0	22·5	375	3·4	0·9	6·5	5·7	60·0	»30	»30	2·0
MEPACRINE	18·3	120	78·0	460	11·8	250	23·5	630	3550	30·0	13·0
ARTEMISININ	10·0	13·8	»30	20·5	7·8	165	6·5	22·5	200	120	11·5
PYRONARIDINE	1·2	1·4	>100	33·5	1·4	19·5	2·2	3·2	14·3	46·0	1·1
PYRIMETHAMINE	0·13	0·08	0·18	0·37	0·21	0·05	0·43	0·03	0·12	0·06	0·09
SULFADOXINE	0·26	0·08	0·21	0·08	0·14	0·05	0·13	<0·3	<0·3	<0·3	0·18
FANSIDAR	0·1	0·14	0·19	0·08	0·1	0·05	0·1	<0·03	0·1	0·05	0·04
CYCLOGUANIL	6·9	4·8	6·8	11·5	5·0	6·3	2·4	3·1	2·5	2·2	12·3
MENOCTONE	4·5	3·1	3·8	4·3	3·5	1·2	3·0	2·0	2·2	2·7	3·2
FLOXACRINE	0·6	0·5	0·5	0·6	0·4	0·3	0·12	0·6	0·5	0·4	0·3
CLINDAMYCIN	55·0	18·5	14·0	24·0	24·0	10·0	14·0	32·0	20·0	31·0	28·5
DOXYCYCLINE	98·0	28·0	17·0	28·0	34·0	32·0	15·5	58·0	42·0	13·8	37·5
LON 1765	6·0	8·2	18·0	56·0	11·2	125	220	10·6	18·0	70·0	5·4

Table 23. ED_{90} values of some antimalarial drugs against resistant lines of P. yoelii ssp. and P.y. nigeriensis (NIG).

	NS	NS1100	SH	SPN	NS1708	ART	NS1765	SAM	MPS	QMS	NIG
CHLOROQUINE	1·0	0·5	1·4	3·9	0·4	7·1	3·8	9·3	8·6	11·6	0·1
AMODIAQUINE	1·0	0·3	>5·6	23·3	1·7	17·2	4·4	6·2	28·3	5·6	0·4
WR 228258	1·0	31·0	0·1	53·8	43·1	»10·3	48·3	>34·5	»34·5	50·0	0·26
PRIMAQUINE	1·0	2·2	1·1	1·6	1·1	1·4	1·2	26·2	1·1	2·4	2·3
QUININE	1·0	2·1	0·7	3·2	0·7	1·4	0·9	3·7	29·3	3·2	0·8
CINCHONINE	1·0	0·3	»2·7	7·3	0·7	3·2	1·2	3·0	14·5	»2·7	0·5
QUINIDINE	1·0	1·2	5·4	5·1	0·4	2·0	0·6	2·5	3·2	27·7	0·6
MEFLOQUINE	1·0	88·9	»13·9	2·8	1·0	9·0	1·5	17·8	25·0	»13·9	0·7
HALOFANTRINE	1·0	22·5	375	3·4	0·9	6·5	5·7	60·0	»30	»30	2·0
MEPACRINE	1·0	6·6	4·3	25·1	0·6	13·7	1·3	34·4	194	1·6	0·7
ARTEMISININ	1·0	1·4	»3·0	2·1	0·8	16·5	0·7	2·3	20·0	12·0	1·2
PYRONARIDINE	1·0	1·2	>83·3	27·9	1·2	16·3	1·8	2·7	11·9	38·3	0·9
PYRIMETHAMINE	1·0	0·6	1·4	2·8	1·6	0·4	3·3	0·2	0·9	0·5	0·7
SULFADOXINE	1·0	0·3	0·8	0·3	0·5	0·2	0·5	<1·2	<1·2	<1·2	0·7
FANSIDAR	1·0	1·4	1·9	0·8	1·0	0·5	1·0	<0·3	1·0	0·5	0·4
CYCLOGUANIL	1·0	0·7	1·0	1·7	0·7	0·9	0·3	0·4	0·4	0·3	1·8
MENOCTONE	1·0	0·7	0·8	1·0	0·8	0·3	0·7	0·4	0·5	0·6	0·7
FLOXACRINE	1·0	0·8	0·8	1·0	0·7	0·5	0·2	0·9	0·8	0·7	0·5
CLINDAMYCIN	1·0	0·3	0·3	0·4	0·4	0·2	0·3	0·6	0·4	0·6	0·5
DOXYCYCLINE	1·0	0·3	0·2	0·3	0·3	0·3	0·2	0·3	0·4	0·1	0·4
LON 1765	1·0	1·4	3·0	9·3	1·9	20·8	36·7	1·8	3·0	11·7	0·9

Table 24. I_{90} values of resistant strains of *P. yoelii ssp.* and *P. y. nigeriensis* (NIG) to some antimalarial drugs.

SUMMARY OF BLOOD SCHIZONTOCIDAL (4 DAY TEST) DATA

	Route	P		B		PYR		ORA		MEN		MFY		KFY		PFM	
		ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I
CHLOROQUINE	SC											5.7	1.8	3.9	1.25	20.0	6
AMODIAQUINE	SC															6.2	2
WR 228258	SC	0.25	0.03	0.47	0.05	0.63	0.06	0.4	0.04	0.91	0.09			2.4	0.24	29.0	2.
		N1765		NAM		QM											
		ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I
CHLOROQUINE	SC			270	87.1												
AMODIAQUINE	SC			350	135												
	SC																

Table 25

ED_{50} / ED_{90} = mg/kg x 4 MTD = maximum tolerated dose

SUMMARY OF BLOOD SCHIZONTOCIDAL (4 DAY TEST) DATA

	Route	NS		SH		SPN		NS1708		ART		NS1765		SAM		MPS	
		ED 50	ED 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I
CHLOROQUINE	SC													520	9.3	480	8
AMODIAQUINE	SC													112	6.2	510	2
	SC																
		QMS		NIG													
		ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I
CHLOROQUINE	SC	650	11.6														
AMODIAQUINE	SC	>100	>5.6														
WR 228258	SC			0.75	0.26												

Table 26

ED_{50} / ED_{90} = mg/kg x 4 MTD = maximum tolerated dose

SUMMARY OF BLOOD SCHIZONTOCIDAL (4 DAY TEST) DATA

	Route	MEN		MFY		KFY		PFMA		NAM		QM					
		ED 50	ED 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I
PRIMAQUINE	sc			20.5	4.3	10.5	2.2	20.5	4.3	45.0	9.4						
QUININE	po			180	1.5	130	1.1	165	1.4	850	7.2						
CINCHONINE	po							17500	140	600	4.8						
		SAM		MPS		QMS											
		ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I
PRIMAQUINE	sc	220	26.2	9.5	1.1	20.0	2.4										
QUININE	po	1080	3.7	8500	29.3	925	3.2										
CINCHONINE	po	660	3.0	3200	14.5	»600	»2.7										

Table 27

ED_{50} / ED_{90} = mg/kg x 4 MTD = maximum tolerated dose

SUMMARY OF BLOOD SCHIZONTOCIDAL (4 DAY TEST) DATA

	Route	MEN		MFY		KFY		PFMA		NAM		Q					
		ED 50	ED 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I
QUINIDINE	po	155	5.0														
MEFLOQUINE	po			10.0	2.2	4.0	0.9	7.7	1.7	95.0	20.7						
MEPACRINE	sc	4.8	2.5							410	216	190	100				
		SAM		MPS		QMS		SPN									
		ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I
QUINIDINE	sc																
MEFLOQUINE	po	128	17.8	180	25.0	>100	>13.9										
MEPACRINE	sc	630	34.4	3550	194	30.0	1.6	460	25.1								

Table 28

ED_{50} / ED_{90} = mg/kg x 4 MTD = maximum tolerated dose

SUMMARY OF BLOOD SCHIZONTOCIDAL (4 DAY TEST) DATA

	Route	MFY		KFY		PFMA		N1765		NAM		QM				NIG	
		ED 50	ED 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I
PYRONARIDINE	sc					1.2	1.7			2.6	3.7	9.0	12.9			1.1	0
PYRIMETHAMINE	ip							1.2	10.0							0.09	0
SULFADOXINE	sc	3.7	0.8	57.0	13.0	<0.3	<0.07			<0.3	<0.07						

		NS		SH		SPN		NS1708		NS1765		SAM		MPS		QMS	
		ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I
PYRONARIDINE	sc																
PYRIMETHAMINE	ip	0.13	1.0	0.18	1.4	0.37	2.8	0.21	1.6	0.43	3.3	0.03	0.2	0.12	0.9	0.06	0
SULFADOXINE	sc											<0.3	<1.2	<0.3	<1.2	<0.3	<1

ED_{50} / ED_{90} = mg/kg x 4 MTD = maximum tolerated dose

Table 29

SUMMARY OF BLOOD SCHIZONTOCIDAL (4 DAY TEST) DATA

	Route	MFY		KFY		PFMA		NAM		QM		MEN					
		ED 50	ED 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 9
FANSIDAR	SC	38.0	119	37.0	116			0.05	0.2								
CYCLOGUANIL	SC	1000	303	70.0	21.2	1.9	0.6	26.0	7.9								
MENOCTONE	SC	1.6	1.1	2.5	1.8	2.0	1.4	2.0	1.4	2.9	2.1	3700	2643				
		SAM		MPS		QMS		NIG									
		ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{9}
FANSIDAR	SC	<0.03	<0.3	0.1	1.0	0.05	0.5										
CYCLOGUANIL	SC	3.1	0.4	2.5	0.4	2.2	0.3										
MENOCTONE	SC	2.0	0.4	2.2	0.5	2.7	0.6	3.2	0.7								

Table 30

ED_{50} / ED_{90} = mg/kg x 4 MTD = maximum tolerated dose

SUMMARY OF BLOOD SCHIZONTOCIDAL (4 DAY TEST) DATA

	Route	MFY		KFY		PFMA		NAM		QM		N1708					
		ED 50	ED 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	I 90	ED 90	
FLOXACRINE	SC	0.5	0.5	0.45	0.45												
CLINDAMYCIN	SC	19.5	0.5	28.0	0.8	16.5	0.5	18.5	0.5	13.8	0.4						
DOXYCYCLINE	SC	32.0	11.9									18.5	6.9				
		NS		SAM		mPS		QMS		NIG		SPN					
		ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I_{90}	ED_{90}	I
FLOXACRINE	SC			0.55	0.9	0.5	0.8	0.4	0.7								
CLINDAMYCIN	SC			32.0	0.6	20.0	0.4	31.0	0.6	28.5	0.5						
DOXYCYCLINE	SC	98.0	1.0							37.5	0.4	28.0	0.3				

Table 31

ED_{50} / ED_{90} = mg/kg x 4 MTD = maximum tolerated dose

SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES) TABLE 32

COMPOUND NAME OR NUMBER CHLOROQUINE..... PARASITE (SUB)SPECIES P. berghei.....

FORMULATION Tween 80/H2O.. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	1.0	5		-	83.9 ± 5.4
	3.0	5		-	43.8 ± 8.5
MFY	10.0	5	1	-	3.1 ± 0.2
	30.0	6		-	0.02 ± 0.0
	60.0	5		-	0
	∅	10		8.6	

ED_{50}(range)	2.3(1.7 - 3.0)
ED_{90}(range)	5.7(4.4-7.6)
Resistance factor I_{90}	

ED_{50}(range)	
ED_{90}(range)	
Resistance factor I_{90}	

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 33

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME

OR NUMBER Chloroquine..... PARASITE (SUB)SPECIES P. berghei.....

FORMULATION Tween 80./H_2O.. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	3.0	5		-	11.9 ± 2.9
	10.0	5		-	3.3 ± 1.4
KFY	30.0	5	1	-	0.3 ± 0.3
	100.0	5		-	0
	Ø	10		6.7	

ED_{50}(range) 0.6 (0.2 - 0.9)

ED_{90}(range) 3.9 (1.0 - 5.7)

Resistance factor I_{90}

	3.0	5		-	91.7 ± 19.2
	10.0	5		-	28.6 ± 8.8
PFMA	30.0	5	1	-	13.1 ± 11.6
	100.0	5		-	0
	Ø	10		6.3	

ED_{50}(range) 9.0 (5.5 - 19.0)

ED_{90}(range) 20.0 (12.5 - 43.0)

Resistance factor I_{90}

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SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES) TABLE 34

COMPOUND NAME OR NUMBER Chloroquine..... PARASITE (SUB)SPECIES P. berghei.....

FORMULATION Tween 80 / H_2O... ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	3.0	5		-	50.0 ± 7.1
	10.0	5		-	39.2 ± 10.0
NAM	30.0	5	1	-	25.3 ± 6.2
	100.0	5		-	17.2 ± 5.5
	Ø	10		10.6	

ED_{50}(range)	3.0(1.3-7.5)
ED_{90}(range)	270(120-650)
Resistance factor I_{90}	

ED_{50}(range)	
ED_{90}(range)	
Resistance factor I_{90}	

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SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES) TABLE 35

COMPOUND NAME OR NUMBER Chloroquine..... PARASITE (SUB)SPECIES P.yoelii ssp....

FORMULATION .Tween 80/H_2O.. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	3.0	5		-	72.9 ± 1.8
	10.0	5		-	63.5 ± 3.9
SAM	30.0	5	1	-	32.7 ± 10.6
	100.0	5		-	26.2 ± 5.1
	Ø	10		23.8	

ED_{50}(range)	14.0(3.3 - 34.0)
ED_{90}(range)	520(125 - >1000)
Resistance factor I_{90}	

	3.0	5		-	85.8 ± 11.6
	10.0	5		-	62.2 ± 6.4
MPS	30.0	5	1	-	50.1 ± 8.5
	100.0	5		-	44.3 ± 0.8
	Ø	10		9.3	

ED_{50}(range)	30.0(13.0 - 80.0)
ED_{90}(range)	480(210 - >1000)
Resistance factor I_{90}	

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES)

TABLE 36

COMPOUND NAME OR NUMBER ..CHLOROQUINE..... PARASITE (SUB)SPECIES .P.yoelii ssp..

FORMULATION .Tween 80/H_2O.. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	1·0	5		-	100 ± 9·8
	3·0	5		-	79·6 ± 10·2
QMS	10·0	5	1	-	56·7 ± 18·0
	30·0	5		-	53·9 ± 8·6
	60·0	5		-	36·3 ± 12·5
	Ø	10		4·9	

ED_{50}(range)	22·0(4·6-70·0)
ED_{90}(range)	650(140->1000)
Resistance factor I_{90}	

ED_{50}(range)	
ED_{90}(range)	
Resistance factor I_{90}	

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
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SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES) TABLE 37

COMPOUND NAME OR NUMBER Amodiaquine PARASITE (SUB)SPECIES P.berghei

FORMULATION Tween 80/H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	3.0	5		-	79.0 ± 18.6
	10.0	5		-	0.7 ± 0.6
PFMA	30.0	5	1	-	0
	100.0	5		-	0
	Ø	10		6.3	
ED_{50}(range) 3.9(3.1 - 11.3)					
ED_{90}(range) 6.2(4.9 - 18.0)					
Resistance factor I_{90}					
	3.0	5		-	77.7 ± 4.0
	10.0	5		-	38.1 ± 11.6
NAM	30.0	5	1	-	30.4 ± 7.8
	100.0	5		-	30.6 ± 6.5
	Ø	10		10.6	
ED_{50}(range) 11.5(1.8 - 40.0)					
ED_{90}(range) 350(55.0->1000)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES) TABLE 38

COMPOUND NAME OR NUMBER Amodiaquine..... PARASITE (SUB)SPECIES P.yoelii.ssp...

FORMULATION Tween 80 / H_2O. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	3.0	5		-	95.3 ± 2.7
	10.0	5		-	67.4 ± 1.5
SAM	30.0	5	1	-	31.3 ± 8.2
	100.0	5		-	17.8 ± 4.1
	Ø	10		23.8	
ED_{50}(range) 19.5(10.5 - 48.0)					
ED_{90}(range) 112(59.0 - 265)					
Resistance factor I_{90}					
	3.0	5		-	77.6 ± 8.3
	10.0	5		-	67.3 ± 5.0
MPS	30.0	5	1	-	49.5 ± 3.9
	100.0	5		-	40.2 ± 6.8
	Ø	10		9.3	
ED_{50}(range) 26.0(9.3 - 80.0)					
ED_{90}(range) 510(180 - >1000)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 39

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME

OR NUMBER Amodiaquine PARASITE (SUB)SPECIES P.yoelii ssp.

FORMULATION Tween 80/H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	3.0	5		-	100 ± 7.5
	10.0	5		-	100 ± 5.2
QMS	30.0	5	1	-	68.1 ± 10.3
	100.0	5		-	60.9 ± 9.2
	Ø	10		6.7	

ED_{50}(range)	> 100
ED_{90}(range)	» 100
Resistance factor I_{90}	

ED_{50}(range)	
ED_{90}(range)	
Resistance factor I_{90}	

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES) TABLE 40

COMPOUND NAME WR 228258 AH (BJ 30663)

OR NUMBER LON.1708 PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80/H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.03	5		-	100 ± 0.7
	0.1	5		-	87.6 ± 8.6
PFMA	0.3	5	1	-	74.5 ± 13.5
	1.0	5		-	70.3 ± 13.2
	3.0	5		-	57.9 ± 15.2
	Ø	10		2.9	
ED_{50}(range) 2.1 (0.5 - 10.8)					
ED_{90}(range) 29.0 (7.0 - >100)					
Resistance factor I_{90}					
	0.03	5		-	92.3 ± 5.6
	0.1	5		-	84.7 ± 4.0
P	0.3	5	1	-	1.6 ± 0.6
	1.0	5		-	0
	3.0	5		-	0
	Ø	10		10.0	
ED_{50}(range) 0.11 (0.06 - 0.22)					
ED_{90}(range) 0.25 (0.14 - 0.5)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES) TABLE 41

COMPOUND NAME WR 228258 AH (BJ 30663)

OR NUMBER LON 1708 PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80/H_2O. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.03	5		-	100
	0.1	5		-	99.4 ± 5.1
B	0.3	5	1	-	4.5 ± 2.6
	1.0	5		-	3.0 ± 1.2
	3.0	5		-	0
	Ø	10		9.4	
ED_{50}(range) 0.27 (0.12 - 0.48)					
ED_{90}(range) 0.47 (0.21 - 0.82)					
Resistance factor I_{90}					
	0.03	5		-	100 ± 9.6
	0.1	5		-	88.9 ± 8.0
PYR	0.3	5	1	-	20.2 ± 4.7
	1.0	5		-	12.7 ± 2.8
	3.0	5		-	0
	Ø	10		8.2	
ED_{50}(range) 0.29 (0.16 - 0.55)					
ED_{90}(range) 0.63 (0.35 - 1.2)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 42

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME WR 228258 AH (BJ 30663)

OR NUMBER LON.1708 PARASITE (SUB)SPECIES P.berghei

FORMULATION Tween 80/H_2O. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.03	5		–	89.7 ± 5.3
	0.1	5		–	82.0 ± 7.8
ORA	0.3	5	1	–	8.1 ± 1.9
	1.0	5		–	1.5 ± 0.3
	3.0	5		–	0.15 ± 0.1
	Ø	10		17.1	
ED_{50}(range) 0.11 (0.06 – 0.37)					
ED_{90}(range) 0.4 (0.23 – 1.4)					
Resistance factor I_{90}					
	0.03	5		–	100 ± 1.2
	0.1	5		–	97.3 ± 2.1
MEN	0.3	5	1	–	33.4 ± 5.2
	1.0	5		–	18.0 ± 3.5
	3.0	5		–	0.6 ± 0.2
	Ø	10		32.4	
ED_{50}(range) 0.36 (0.19 – 0.56)					
ED_{90}(range) 0.91 (0.47 – 1.4)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES)

TABLE 43

COMPOUND NAME WR 228258 AH (BJ 30663)

OR NUMBER LON 1708 PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80/H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.03	5		-	100 ± 3.6
	0.1	5		-	78.0 ± 12.4
KFY	0.3	5	1	-	44.3 ± 11.1
	1.0	5		-	30.5 ± 11.3
	3.0	5		-	14.1 ± 4.5
	Ø	10		14.9	

ED_{50}(range)	0.35 (0.15 - 0.76)
ED_{90}(range)	2.4 (1.0 - 5.2)
Resistance factor I_{90}	

ED_{50}(range)	
ED_{90}(range)	
Resistance factor I_{90}	

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 44

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME WR 228258 AH (BJ 30663)

OR NUMBER LON 1708 PARASITE (SUB)SPECIES P.y.nigeriensis

FORMULATION Tween 80/H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.03	5		-	95.7 ± 1.7
	0.1	5		-	92.3 ± 3.7
NIG	0.3	5	1	-	45.5 ± 5.4
	1.0	5		-	30.2 ± 5.0
	3.0	5		-	0.15 ± 0.07
	Ø	10		27.2	

ED_{50}(range)	0.27 (0.1 - 0.76)
ED_{90}(range)	0.75 (0.29 - 2.1)
Resistance factor I_{90}	

ED_{50}(range)	
ED_{90}(range)	
Resistance factor I_{90}	

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 45

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME

OR NUMBER Primaquine PARASITE (SUB)SPECIES P.berghei

FORMULATION Tween 80/H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X10
	1.0	5		-	60.6 ± 10.8
	3.0	5		-	54.3 ± 10.4
MFY	10.0	5	1	-	46.1 ± 9.6
	30.0	5		-	6.6 ± 2.7
	Ø	10		9.8	
ED_{50}(range) 3.4(1.0 - 12.0)					
ED_{90}(range) 20.5(5.9 - 73.0)					
Resistance factor I_{90}					
	1.0	5		-	100 ± 1.5
	3.0	5		-	89.5 ± 15.7
KFY	10.0	6	1	-	30.0 ± 9.6
	30.0	5		-	0.02 ± 0.0
	Ø	10		8.8	
ED_{50}(range) 5.8(2.7 - 8.5)					
ED_{90}(range) 10.5(4.9 - 15.8)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES) TABLE 46

COMPOUND NAME OR NUMBER ..Primaquine..... PARASITE (SUB)SPECIES ..P.berghei....

FORMULATION ..Tween.80/.H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	1·0	5		-	100 ± 6·3
	3·0	5		-	87·4 ± 8·9
PFMA	10·0	5	1	-	75·3 ± 12·9
	30·0	5		-	8·8 ± 4·2
	Ø	10		7·3	
ED_{50}(range) 9.5(4.7 - 20.0)					
ED_{90}(range) 20.5(10.0 - 43.0)					
Resistance factor I_{90}					
	1·0	5		-	100 ± 4·7
	3·0	5		-	85·1 ± 6·5
NAM	10·0	5	1	-	73·2 ± 2·1
	30·0	5		-	46·8 ± 9·6
	Ø	10		11·8	
ED_{50}(range) 15.5(5.5 - 35.0)					
ED_{90}(range) 45.0(16.0 - 100)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
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London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES) TABLE 47

COMPOUND NAME OR NUMBER ..Primaquine..... PARASITE (SUB)SPECIES ..P.yoelii ssp..

FORMULATION ..Tween 80 / H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	1.0	5		-	100 ± 3.9
	3.0	5		-	83.8 ± 4.8
SAM	10.0	5	1	-	85.7 ± 18.6
	30.0	5		-	38.8 ± 11.2
	Ø	10		9.9	

ED_{50}(range)	23.0(11.0 - 95.0)
ED_{90}(range)	220(88.0 - 640)
Resistance factor I_{90}	

ED_{50}(range)	
ED_{90}(range)	
Resistance factor I_{90}	

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 48

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME

OR NUMBER PRIMAQUINE..... PARASITE (SUB)SPECIES P.yoelii ssp....

FORMULATION Tween 80/H_2O... ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	1.0	5		-	100 ± 0.5
	3.0	5		-	97.4 ± 8.8
QMS	10.0	5	1	-	52.4 ± 19.1
	30.0	5		-	2.9 ± 1.6
	∅	10		3.5	
ED_{50}(range) 9.5(5.9 - 14.0)					
ED_{90}(range) 20.0(12.8 - 31.0)					
Resistance factor I_{90}					
	1.0	5		-	54.4 ± 11.1
	3.0	5		-	40.2 ± 9.4
MPS	10.0	5	1	-	24.8 ± 6.9
	30.0	5		-	1.2 ± 0.4
	∅	10		10.0	
ED_{50}(range) 2.2(0.8 - 5.6)					
ED_{90}(range) 9.5(3.4 - 23.5)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES) TABLE 49

COMPOUND NAME OR NUMBER ..QUININE HCl..... PARASITE (SUB)SPECIES .P. berghei....

FORMULATION ..Tween 80/H_2O ROUTE OF ADMINISTRATION : ~~SC/IP~~/PO/~~IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	30.0	5		-	79.4 ± 7.4
	100.0	5		-	38.6 ± 14.3
MFY	300.0	5	1	-	24.7 ± 2.4
	600.0	5		-	0.08 ± 0.0
	Ø	10		9.8	
ED_{50}(range) 80.0(42.0-200)					
ED_{90}(range) 180(92.0-440)					
Resistance factor I_{90}					
	30.0	5		-	95.2 ± 3.7
	100.0	5		-	13.2 ± 3.1
KFY	300.0	5	1	-	1.6 ± 1.1
	600.0	5		-	0
	Ø	10		8.8	
ED_{50}(range) 60.0(44.0-90.0)					
ED_{90}(range) 130(95.0-195)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 50
(BLOOD SCHIZONTOCIDES)

COMPOUND NAME
OR NUMBER QUININE HCl ..... PARASITE (SUB)SPECIES P. berghei .....

FORMULATION Tween 80/H_2O ... ROUTE OF ADMINISTRATION : ~~SC/IP~~/PO/~~IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	30.0	5		-	100 ± 6.3
	100.0	5		-	77.3 ± 8.4
PFMA	300.0	5	1	-	0.03 ± 0.03
	600.0	5		-	0
	Ø	10		7.3	
ED_{50} (range) 80.0 (36.0 - 175)					
ED_{90} (range) 165 (72.0 - 360)					
Resistance factor I_{90}					
	30.0	5		-	99.3 ± 4.4
	100.0	5		-	65.3 ± 4.7
NAM	300.0	5	1	-	30.8 ± 3.3
	600.0	5		-	26.0 ± 11.8
	Ø	10		11.8	
ED_{50} (range) 245 (125 - 430)					
ED_{90} (range) 850 (430 - 1500)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES) TABLE 51

COMPOUND NAME OR NUMBER ..QUININE HCL..... PARASITE (SUB)SPECIES ..P.yoelii ssp..

FORMULATION ..Tween 80 /H_2O.. ROUTE OF ADMINISTRATION : ~~SC/IP/~~PO~~/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	30·0	5		-	100 ± 4.5
	100·0	5		-	100 ± 13·6
SAM	300·0	5	1	-	62.4 ± 13.4
	600·0	5		-	51.3 ± 9.9
	Ø	10		9.9	

ED_{50}(range)	450(280-720)
ED_{90}(range)	1080(660-1700)
Resistance factor I_{90}	

ED_{50}(range)	
ED_{90}(range)	
Resistance factor I_{90}	

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES) TABLE 52

COMPOUND NAME OR NUMBER Quinine Hydrochloride... PARASITE (SUB)SPECIES P. yoelii ssp...

FORMULATION Tween80/H_2O... ROUTE OF ADMINISTRATION : ~~SC/IP~~/PO/~~IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	30.0	5		-	78.4 ± 11.9
	100.0	5		-	61.6 ± 9.6
MPS	300.0	5	1	-	55.8 ± 12.4
	600.0	5		-	39.3 ± 12.4
	Ø	10		10.0	
ED_{50}(range) 265(110 - 1050)					
ED_{90}(range) 8500(3500 - >10000)					
Resistance factor I_{90}					
	30.0	5		-	100
	100.0	5		-	84.9 ± 14.2
QMS	300.0	5	1	-	84.3 ± 11.5
	600.0	5		-	39.0 ± 27.0
	Ø	10		3.5	
ED_{50}(range) 360(145 - 800)					
ED_{90}(range) 925(375 - 2000)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES) TABLE 53

COMPOUND NAME OR NUMBER CINCHONINE HYDROCHLORIDE PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80 / H_2O ... ROUTE OF ADMINISTRATION : ~~SC/IP~~/PO/~~IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	30.0	5		-	88.6 ± 4.4
	100.0	5		-	85.6 ± 10.2
PFMA	300.0	5	1	-	72.0 ± 5.1
	600.0	5		-	61.4 ± 10.9
	∅	10		2.6	
ED_{50}(range) 1050 (440 - 4200)					
ED_{90}(range) 17500 (780 - 70000)					
Resistance factor I_{90}					
	30.0	5		-	100 ± 5.8
	100.0	5		-	71.5 ± 14.7
NAM	300.0	5	1	-	49.7 ± 12.1
	600.0	5		-	7.0 ± 2.5
	∅	10		8.9	
ED_{50}(range) 225 (110 - 370)					
ED_{90}(range) 600 (295 - 1020)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
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London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 54

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME

OR NUMBER CINCHONINE HYDROCHLORIDE PARASITE (SUB)SPECIES ...P.yoelii ssp...

FORMULATION Tween 80 / H_2O ROUTE OF ADMINISTRATION : ~~SC/IP~~/PO/~~IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	30.0	5		-	75.1 ± 7.3
	100.0	5		-	75.3 ± 7.2
SAM	300.0	5	1	-	44.8 ± 12.4
	600.0	5		-	8.4 ± 2.3
	ø	10		24.4	

ED_{50} (range) 215 (150 - 350)

ED_{90} (range) 660 (460 - 1080)

Resistance factor I_{90}

	30.0	5		-	84.2 ± 5.8
	100.0	5		-	59.2 ± 12.1
MPS	300.0	5	1	-	38.8 ± 11.1
	600.0	5		-	36.4 ± 10.9
	ø	15		10.0	

ED_{50} (range) 190 (72.0 - 500)

ED_{90} (range) 3200 (1250 - 8000)

Resistance factor I_{90}

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
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SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES)

TABLE 55

COMPOUND NAME OR NUMBER CINCHONINE Hydrochloride PARASITE (SUB)SPECIES P. yoelii ssp...

FORMULATION Tween 80/H_2O.. ROUTE OF ADMINISTRATION : ~~SC/IP~~/PO/~~IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	30.0	5		-	100 ±
	100.0	5		-	98.6 ± 3.8
QMS	300.0	5	1	-	100 ± 6.6
	600.0	5		-	100 ± 4.4
	ø	10		3.5	

ED_{50}(range)	
ED_{90}(range) NA 600	
Resistance factor I_{90}	

ED_{50}(range)	
ED_{90}(range)	
Resistance factor I_{90}	

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 56

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME

OR NUMBER QUINIDINE HYDROCHLORIDE PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80 / H_2O. ROUTE OF ADMINISTRATION : ~~SC/IP~~/PO/~~IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	30.0	5		-	65.8 ± 11.4
	100.0	5		-	21.7 ± 16.2
MEN	300.0	5	1	-	0
	600.0	5		-	0
	∅	10		10.3	

ED_{50}(range)	43.0 (32.0 - 72.0)
ED_{90}(range)	155 (115 - 260)
Resistance factor I_{90}	

ED_{50}(range)	
ED_{90}(range)	
Resistance factor I_{90}	

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES) TABLE 57

COMPOUND NAME OR NUMBER .MEFLOQUINE..... PARASITE (SUB)SPECIES .P.berghei.....

FORMULATION .Tween 80./H_2O... ROUTE OF ADMINISTRATION : ~~SC/IP~~/PO/~~IV~~

MAXIMUM TOLERATED DOSE (MTD) ~.100. MG/KG X 4.

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	3.0	5		-	64.5 ± 10.6
	10.0	5		-	2.7 ± 1.7
MFY	30.0	5	1	-	0.4 ± 0.2
	100.0	5		-	0.08 ± 0.0
	Ø	10		16.1	

ED_{50}(range) 2.7(1.0 - 5.9)

ED_{90}(range) 10.0(3.5 - 21.5)

Resistance factor I_{90}

	3.0	5		-	23.8 ± 16.6
	10.0	5		-	0.3 ± 0.2
KFY	30.0	5	1	-	0
	100.0	5		-	0
	Ø	10		9.5	

ED_{50}(range) 1.9(1.2 - 2.6)

ED_{90}(range) 4.0(2.6 - 5.6)

Resistance factor I_{90}

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 58

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME

OR NUMBER MEFLOQUINE..... PARASITE (SUB)SPECIES P.berghei.....

FORMULATION Tween 80/H_2O.. ROUTE OF ADMINISTRATION : ~~SC/IP~~/PO/~~IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X10(
	3.0	5		-	100 ± 2.6
	10.0	5		-	0.7 ± 0.6
PFMA	30.0	5	1	-	0
	100.0	5		-	0
	Ø	10		9.7	
ED_{50}(range) 6.0(5.2 - 6.9)					
ED_{90}(range) 7.7(6.6 - 8.8)					
Resistance factor I_{90}					
	3.0	5		-	51.8 ± 7.7
	10.0	5		-	45.2 ± 7.6
NAM	30.0	5	1	-	20.4 ± 1.1
	100.0	5		-	13.5 ± 3.9
	Ø	10		18.5	
ED_{50}(range) 4.7(2.0 - 12.0)					
ED_{90}(range) 95.0(41.0 - 235)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES) TABLE 59

COMPOUND NAME OR NUMBER .MEFLOQUINE..... PARASITE (SUB)SPECIES .P.yoelii ssp...

FORMULATION .Tween 80/H_2O.. ROUTE OF ADMINISTRATION : ~~SC/IP~~/PO/~~IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	3.0	5		-	60.0 ± 6.3
	10.0	5		-	40.8 ± 6.6
SAM	30.0	5	1	-	24.0 ± 7.8
	100.0	5		-	12.9 ± 3.4
	Ø	10		20.6	
ED_{50}(range) 5.4(2.8-9.6)					
ED_{90}(range) 128(66.0-240)					
Resistance factor I_{90}					
	3.0	5		-	100 ± 3.3
	10.0	5		-	98.2 ± 3.5
MPS	30.0	5	1	-	66.5 ± 16.3
	100.0	5		-	60.7 ± 3.5
	Ø	10		9.8	
ED_{50}(range) 63.0(29.0-138)					
ED_{90}(range) 180(87.0-400)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
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London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES)

TABLE 60

COMPOUND NAME OR NUMBER ..MEFLOQUINE..... PARASITE (SUB)SPECIES P. yoelii spp..

FORMULATION .Tween 80/H_2O. ROUTE OF ADMINISTRATION : ~~SC/IP~~/PO/~~IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X10(
	3.0	5		-	97.3 ± 12.7
	10.0	5		-	90.0 ± 8.7
QMS	30.0	5	1	-	84.1 ± 10.5
	100.0	5		-	78.2 ± 7.0
	Ø	10		4.4	

ED_{50}(range)	>100
ED_{90}(range)	» 100
Resistance factor I_{90}	

ED_{50}(range)	
ED_{90}(range)	
Resistance factor I_{90}	

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
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SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES) TABLE 61

COMPOUND NAME OR NUMBER MEPACRINE..... PARASITE (SUB)SPECIES P. berghei.....

FORMULATION ..Tween 80/H_2O.. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.3	5		-	100 ± 0.7
	1.0	5		-	83.9 ± 2.1
MEN	3.0	5	1	-	71.7 ± 4.5
	10.0	5		-	0.6 ± 0.4
	30.0	5		-	0
	∅	10		10.3	
ED_{50}(range) 2.3(1.6 - 4.4)					
ED_{90}(range) 4.8(3.3 - 9.0)					
Resistance factor I_{90}					
	10.0	5		-	100 ± 11.4
	30.0	5		-	78.8 ± 14.4
Q	60.0	5	1	-	40.8 ± 16.6
	100.0	5		-	34.6 ± 12.2
	∅	10			
ED_{50}(range) 83.0(37.0 - 280)					
ED_{90}(range) 190(82.0 - 640)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES)

TABLE 62

COMPOUND NAME OR NUMBER MEPACRINE PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80/H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	10.0	5		-	48.9 ± 3.9
	30.0	5		-	35.2 ± 6.4
NAM	60.0	5	1	-	26.1 ± 3.4
	100.0	5		-	22.3 ± 6.8
	Ø	10		26.2	

ED_{50}(range)	9.0(4.0-15.5)
ED_{90}(range)	410(190-700)
Resistance factor I_{90}	

ED_{50}(range)	
ED_{90}(range)	
Resistance factor I_{90}	

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 63

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME

OR NUMBER MEPACRINE..... PARASITE (SUB)SPECIES P.yoelii ssp....

FORMULATION Tween 80/H_2O.... ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.3	5		-	94.2 ± 12.4
	1.0	5		-	58.8 ± 9.7
QMS	3.0	5	1	-	44.8 ± 6.8
	10.0	5		-	27.1 ± 4.4
	30.0	5		-	20.6 ± 6.2
	Ø	10		6.5	
ED_{50}(range) 2.7(0.9 - 9.3)					
ED_{90}(range) 30.0(10.2 - 100)					
Resistance factor I_{90}					
	10.0	5		-	100 ± 1.5
	30.0	5		-	93.1 ± 9.7
SPN	60.0	5	1	-	77.3 ± 16.9
	100.0	5		-	61.1 ± 10.8
	Ø	10		7.5	
ED_{50}(range) 125(93.0 - 175)					
ED_{90}(range) 460(340 - 640)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES) TABLE 64

COMPOUND NAME OR NUMBER MEPACRINE PARASITE (SUB)SPECIES P. yoelii ssp.

FORMULATION Tween 80 / H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	10.0	5		-	100 ± 3.9
	30.0	5		-	92.6 ± 6.8
MPS	60.0	5	1	-	87.4 ± 9.5
	100.0	5		-	77.8 ± 7.1
	Ø	10		7.3	

ED_{50} (range) 390 (245 - 600)

ED_{90} (range) 3550 (2250 - 5500)

Resistance factor I_{90}

	10.0	5		-	67.7 ± 8.6
	30.0	5		-	46.6 ± 6.8
SAM	60.0	5	1	-	39.2 ± 6.5
	100.0	5		-	30.8 ± 3.4
	Ø	10		22.2	

ED_{50} (range) 25.5 (16.5 - 8.7)

ED_{90} (range) 630 (400 - 2000)

Resistance factor I_{90}

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 65

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME OR NUMBER ..PYRONARIDINE..... PARASITE (SUB)SPECIES ..P.berghei.....

FORMULATION ..Tween.80/.H_2O. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X10
	0.3	5		-	100 ± 2.9
	1.0	5		-	12.4 ± 8.0
PFMA	3.0	5	1	-	0.15 ± 0.1
	10.0	5		-	0
	Ø	10		16.4	
ED_{50}(range) 0.7(0.5 - 1.5)					
ED_{90}(range) 1.2(0.8 - 2.6)					
Resistance factor I_{90}					
	0.3	5		-	100
	1.0	5		-	63.1 ± 16.6
NAM	3.0	5	1	-	9.1 ± 4.1
	10.0	5		-	0
	Ø	10		9.3	
ED_{50}(range) 1.2(0.9 - 1.6)					
ED_{90}(range) 2.6(1.9 - 3.4)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES)

TABLE 66

COMPOUND NAME OR NUMBER ..PYRONARIDINE..... PARASITE (SUB)SPECIES ..P. berghei....

FORMULATION ..Tween 80/H_2O... ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.3	5		-	89.7 ± 6.3
	1.0	5		-	53.2 ± 12.4
QM	3.0	5	1	-	19.7 ± 4.6
	10.0	5		-	13.6 ± 3.7
	Ø	10		20.7	

ED_{50}(range)	1.4(0.7 - 3.9)
ED_{90}(range)	9.0(4.3 - 25.0)
Resistance factor I_{90}	

ED_{50}(range)	
ED_{90}(range)	
Resistance factor I_{90}	

Principal Investigator: Professor W.Peters
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London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 67

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME

OR NUMBER .PYRONARIDINE..... PARASITE (SUB)SPECIES P.y.nigeriensis

FORMULATION .Tween.80/H_2O.. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X10
	0.3	5		-	96.0 ± 2.1
	1.0	5		-	24.3 ± 16.7
NIG	3.0	5	1	-	0.008 ± 0.0
	10.0	5		-	0
	Ø	10		25.2	

ED_{50}(range)	0.6(0.5-0.9)
ED_{90}(range)	1.1(0.9-1.6)
Resistance factor I_{90}	

ED_{50}(range)	
ED_{90}(range)	
Resistance factor I_{90}	

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES)

TABLE 68

COMPOUND NAME OR NUMBER ..PYRIMETHAMINE..... PARASITE (SUB)SPECIES .P.berghei.....

FORMULATION .Tween80./H_2O. ROUTE OF ADMINISTRATION : ~~SC~~/IP/~~PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.03	5		-	86.1 ± 5.2
	0.1	5		-	72.6 ± 12.7
N1765	0.3	5	1	-	29.3 ± 9.7
	1.0	5		-	24.4 ± 11.5
	Ø	10		14.4	0

ED_{50}(range)	0.21(0.09 - 0.6)
ED_{90}(range)	1.2(0.5 - 3.4)
Resistance factor I_{90}	

ED_{50}(range)	
ED_{90}(range)	
Resistance factor I_{90}	

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES) TABLE 69

COMPOUND NAME OR NUMBER PYRIMETHAMINE..... PARASITE (SUB)SPECIES P.yoelii.ssp..

FORMULATION Tween 80/H_2O ROUTE OF ADMINISTRATION : ~~SC~~/IP/~~PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.001	5		–	91.0 ± 7.9
	0.003	5		–	85.9 ± 8.7
NS	0.01	5	1	–	70.5 ± 5.8
	0.03	5		–	42.1 ± 7.0
	0.1	5		–	14.7 ± 3.4
	Ø	10		16.3	
ED_{50}(range) 0.015 (0.005 – 0.035)					
ED_{90}(range) 0.13 (0.043 – 0.29)					
Resistance factor I_{90} 1.0					
	0.001	5		–	100 ± 0.3
	0.003	5		–	95.6 ± 3.8
SH	0.01	5	1	–	89.9 ± 6.0
	0.03	5		–	76.6 ± 3.3
	0.1	5		–	31.4 ± 7.2
	Ø	10		17.3	
ED_{50}(range) 0.031 (0.015 – 0.08)					
ED_{90}(range) 0.18 (0.066 – 0.35)					
Resistance factor I_{90} 1.4					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES) TABLE 70

COMPOUND NAME OR NUMBER ..PYRIMETHAMINE.... PARASITE (SUB)SPECIES .P.yoelii.ssp.

FORMULATION .Tween.80./H_2O ROUTE OF ADMINISTRATION : ~~SC~~/IP/~~PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.003	5		-	96.2 ± 5.8
	0.01	5		-	88.4 ± 4.9
SPN	0.03	5	1	-	82.0 ± 7.4
	0.1	5		-	47.2 ± 8.9
	0.3	5		-	13.2 ± 4.9
	Ø	10		17.6	
ED_{50}(range) 0.06(0.02 - 0.175)					
ED_{90}(range) 0.37(0.125 - 1.1)					
Resistance factor I_{90} 2.8					
	0.003	5		-	93.0 ± 4.4
	0.01	5		-	98.0 ± 1.5
NS1708	0.03	5	1	-	76.9 ± 11.9
	0.1	5		-	36.2 ± 11.3
	0.3	5		-	5.5 ± 5.0
	Ø	10		29.0	
ED_{50}(range) 0.064(0.042 - 0.92)					
ED_{90}(range) 0.21(0.135 - 0.3)					
Resistance factor I_{90} 1.6					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES) TABLE 71

COMPOUND NAME OR NUMBER ..PYRIMETHAMINE..... PARASITE (SUB)SPECIES P.yoelii.ssp...

FORMULATION ..Tween 80/H_2O. ROUTE OF ADMINISTRATION : ~~SC~~/IP/~~PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.003	5		-	95.4 ± 0.7
	0.01	5		-	94.9 ± 2.1
NS 1765	0.03	5	1	-	84.1 ± 9.6
	0.1	5		-	59.8 ± 15.7
	0.3	5		-	16.5 ± 4.5
	Ø	10		29.0	
ED_{50}(range) 0.095 (0.055 - 0.24)					
ED_{90}(range) 0.43 (0.25 - 1.1)					
Resistance factor I_{90} 3.3					
	0.003	5		-	93.2 ± 2.3
	0.01	5		-	85.5 ± 5.5
NIG	0.03	5	1	-	59.7 ± 17.1
	0.1	5		-	17.2 ± 12.3
	0.3	5		-	0.8 ± 0.4
	1.0	5		-	0
	Ø	10		29.6	
ED_{50}(range) 0.024 (0.011 - 0.056)					
ED_{90}(range) 0.085 (0.04 - 0.2)					
Resistance factor I_{90} 0.7					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES) TABLE 72

COMPOUND NAME OR NUMBER ..PYRIMETHAMINE..... PARASITE (SUB)SPECIES .P.yoelii.ssp....

FORMULATION .Tween.80./.H_2O.. ROUTE OF ADMINISTRATION : ~~SC~~/IP/~~PO~~/~~IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X10(
	0.03	5		-	6.6 ± 3.4
	0.1	5		-	0.8 ± 0.4
SAM	0.3	5	1	-	0
	1.0	5		-	0
	Ø	10		27.2	

ED_{50}(range) 0.007(0.004 - 0.01)

ED_{90}(range) 0.03(0.02 - 0.04)

Resistance factor I_{90}

	0.1	5		-	26.3 ± 18.6
	0.3	5		-	0.04 ± 0.0
MPS	1.0	5	1	-	0
	3.0	5		-	0
	Ø	10		9.8	

ED_{50}(range) 0.07(0.05 - 0.1)

ED_{90}(range) 0.12(0.09 - 0.16)

Resistance factor I_{90}

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 73

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME

OR NUMBER .PYRIMETHAMINE..... PARASITE (SUB)SPECIES .P. yoelii ssp..

FOPMULATION .Tween 80./H_2O.... ROUTE OF ADMINISTRATION : ~~SC~~/IP/~~PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.03	5		-	62.5 ± 10.7
	0.1	5		-	1.7 ± 1.0
QMS	0.3	5	1	-	0
	1.0	5		-	0
	3.0	5		-	0
	Ø	10		7.3	

ED_{50}(range)	0.035(0.03-0.04)
ED_{90}(range)	0.06(0.05-0.08)
Resistance factor I_{90}	

ED_{50}(range)	
ED_{90}(range)	
Resistance factor I_{90}	

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 74
(BLOOD SCHIZONTOCIDES)

COMPOUND NAME
OR NUMBER .SULFADOXINE..... PARASITE (SUB)SPECIES .P.berghei....
FORMULATION .Tween 80/H_2O. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~
MAXIMUM TOLERATED DOSE (MTD) .>30.. MG/KG X 4..

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X10
	0.3	5		-	72.9 ± 4.0
	1.0	5		-	54.8 ± 12.6
MFY	3.0	5	1	-	20.7 ± 11.0
	10.0	5		-	2.3 ± 1.2
	30.0	5		-	0.06 ± 0.0
	Ø	10		9.5	
ED_{50}(range) 0.8(0.4 - 1.7)					
ED_{90}(range) 3.7(2.0 - 7.8)					
Resistance factor I_{90}					
	0.3	5		-	87.9 ± 4.4
	1.0	5		-	85.4 ± 5.5
KFY	3.0	5	1	-	73.2 ± 6.7
	10.0	5		-	59.8 ± 12.6
	30.0	5		-	20.0 ± 16.8
	Ø	10		11.4	
ED_{50}(range) 7.6(3.6 - 25.5)					
ED_{90}(range) 57.0(27.0 - 190)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
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London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 75
(BLOOD SCHIZONTOCIDES)

COMPOUND NAME
OR NUMBER ..SULFADOXINE..... PARASITE (SUB)SPECIES .P.berghei.....
FORMULATION .Tween 80 /H_2O. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~
MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.3	5		-	0.04 ± 0.0
	1.0	5		-	0
PFMA	3.0	5	1	-	0
	10.0	5		-	0
	30.0	5		-	0
	Ø	10		10.1	
ED_{50}(range) < 0.3					
ED_{90}(range) < 0.3					
Resistance factor I_{90}					
	0.3	5		-	0
	1.0	5		-	0
NAM	3.0	5	1	-	0
	10.0	5		-	0
	30.0	5		-	0
	Ø	10		9.0	
ED_{50}(range) < 0.3					
ED_{90}(range) < 0.3					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 76

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME

OR NUMBER SULFADOXINE..... PARASITE (SUB)SPECIES P.yoelii ssp...

FORMULATION Tween 80/H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.3	5		-	0.007±0.00
	1.0	5		-	0
SAM	3.0	5	1	-	0
	10.0	5		-	0
	Ø	10		27.2	
ED_{50}(range) < 0.3					
ED_{90}(range) < 0.3					
Resistance factor I_{90}					
	1.0	5		-	0.02 ± 0.02
	3.0	5		-	0
MPS	10.0	5	1	-	0
	30.0	5		-	0
	Ø	10		9.8	
ED_{50}(range) < 0.3					
ED_{90}(range) < 0.3					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
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London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES) TABLE 77

COMPOUND NAME OR NUMBER ...SULFADOXINE..... PARASITE (SUB)SPECIES .P.yoelii ssp...

FORMULATION .Tween 80/H_2O... ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.3	5		-	0.03 ± 0.03
	1.0	5		-	0.03 ± 0.03
QMS	3.0	5	1	-	0
	10.0	5		-	0
	30.0	5		-	0
	Ø	10		7.3	

ED_{50}(range)	
ED_{90}(range)	< 0.3
Resistance factor I_{90}	

ED_{50}(range)	
ED_{90}(range)	
Resistance factor I_{90}	

Principal Investigator: Professor W.Peters
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London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 78

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME (1:3)

OR NUMBER PYRIMETHAMINE:SULFADOXINE. PARASITE (SUB)SPECIES P.berghei

FORMULATION Tween 80/H_2O... ROUTE OF ADMINISTRATION : ~~SC~~/IP/~~PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.03	5		-	17.2 ± 7.2
	0.1	5		-	4.3 ± 0.9
NAM	0.3	5	1	-	0.5 ± 0.3
	1.0	5		-	0
	Ø	10		16.9	

ED_{50}(range) 0.01 (0.006-0.016)

ED_{90}(range) 0.05 (0.03-0.08)

Resistance factor I_{90}

ED_{50}(range)

ED_{90}(range)

Resistance factor I_{90}

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 79

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME (1:3)

OR NUMBER PYRIMETHAMINE: SULFADOXINE PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80 / H_2O .. ROUTE OF ADMINISTRATION : ~~SC~~/IP/~~PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.03	5		-	93.0 ± 2.9
	0.1	5		-	97.4 ± 6.0
MFY	0.3	5	1	-	87.9 ± 4.9
	1.0	5		-	70.2 ± 12.3
	3.0	5		-	56.3 ± 16.7
	∅	10		8.6	
ED_{50}(range) 3.1(1.7 - 9.7)					
ED_{90}(range) 38.0(20.5 - 120)					
Resistance factor I_{90}					
	0.03	5		-	100 ± 2.5
	0.1	5		-	95.3 ± 4.5
KFY	0.3	5	1	-	79.7 ± 8.4
	1.0	5		-	71.4 ± 11.0
	3.0	5		-	56.9 ± 8.5
	∅	10		19.5	
ED_{50}(range) 2.9(0.9 - 6.6)					
ED_{90}(range) 37.0(120 - 85.0)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES) TABLE 80

COMPOUND NAME (1:3)
OR NUMBER PYRIMETHAMINE : SULFADOXINE PARASITE (SUB)SPECIES P. yoelii ssp...
FORMULATION Tween 80/H_2O... ROUTE OF ADMINISTRATION : ~~SC~~/IP/~~PO/IV~~
MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.03	5		-	1.0 ± 0.8
	0.1	5		-	0.13 ± 0.1
SAM	0.3	5	1	-	0
	1.0	5		-	0
	Ø	10		18.9	

ED_{50}(range)	< 0.03
ED_{90}(range)	< 0.03
Resistance factor I_{90}	

ED_{50}(range)	
ED_{90}(range)	
Resistance factor I_{90}	

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES) TABLE 81

COMPOUND NAME (1:3)
OR NUMBER PYRIMETHAMINE : SULFADOXINE PARASITE (SUB)SPECIES P. yoelii ssp.
FORMULATION Tween 80/H_2O ... ROUTE OF ADMINISTRATION : ~~SC~~/IP/~~PO/IV~~
MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.03	5		-	53.8 ± 17.8
	0.1	5		-	0.3 ± 0.3
QMS	0.3	5	1	-	0
	1.0	5		-	0
	3.0	5		-	0
	Ø	10		7.3	
ED_{50}(range) 0.03(0.02 - 0.04)					
ED_{90}(range) 0.05(0.04 - 0.06)					
Resistance factor I_{90}					
	0.03	5		-	99.7 ± 100
	0.1	5		-	0.6 ± 0.5
MPS	0.3	5	1	-	0.03 ± 0.03
	1.0	5		-	0
	3.0	5		-	0
	Ø	10		7.5	
ED_{50}(range) 0.06(0.03 - 0.11)					
ED_{90}(range) 0.10(0.05 - 0.18)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES) TABLE 82

COMPOUND NAME OR NUMBER Cycloguanil PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80/H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.3	5		-	75.5 ± 7.8
	1.0	5		-	61.5 ± 8.6
NAM	3.0	5	1	-	35.5 ± 15.8
	10.0	5		-	28.4 ± 15.5
	∅	10		16.9	

ED_{50}(range) 1.8(0.5 - 7.0)

ED_{90}(range) 26.0(7.3 - 100)

Resistance factor I_{90}

	0.3	5		-	100 ± 4.5
	1.0	5		-	93.0 ± 8.0
MFY	3.0	5	1	-	92.7 ± 7.0
	10.0	5		-	68.6 ± 11.5
	∅	10		7.7	

ED_{50}(range) 53.0(15.0 - 210)

ED_{90}(range) 1000(280 -> 1000)

Resistance factor I_{90}

Interpolated graphically

Principal Investigator: Professor W.Peters
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London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES) TABLE 83

COMPOUND NAME OR NUMBER ..Cycloguanil..... PARASITE (SUB)SPECIES .P.berghei.....

FORMULATION .Tween 80 / H_2O.. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.3	5		-	77.4 ± 17.1
	1.0	5		-	49.8 ± 16.6
KFY	3.0	5	1	-	45.9 ± 5.8
	10.0	5		-	42.5 ± 4.9
	Ø	10		13.3	

ED_{50}(range) 2.0 (0.3 - 8.0)

ED_{90}(range) 70.0 (10.0 -> 100) Interpolated graphically

Resistance factor I_{90}

	0.3	5		-	41.2 ± 11.5
	1.0	5		-	15.9 ± 5.5
PFMA	3.0	5	1	-	6.0 ± 0.8
	10.0	5		-	1.9 ± 0.6
	Ø	10		17.9	

ED_{50}(range) 0.2 (0.1 - 0.3)

ED_{90}(range) 1.9 (1.1 - 3.5)

Resistance factor I_{90}

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES) TABLE 84

COMPOUND NAME OR NUMBER ..CYCLOGUANIL..... PARASITE (SUB)SPECIES P. yoelii ssp...

FORMULATION ..Tween 80/H_2O. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X10C
	0.3	5		-	95.0 ± 5.1
	1.0	5		-	39.9 ± 15.9
SAM	3.0	5	1	-	22.8 ± 6.5
	10.0	5		-	0.4 ± 0.2
	Ø	10		18.9	
ED_{50}(range) 1.1(0.5 - 2.0)					
ED_{90}(range) 3.1(1.5 - 5.5)					
Resistance factor I_{90}					
	0.3	5		-	49.1 ± 9.1
	1.0	5		-	21.4 ± 7.6
MPS	3.0	5	1	-	7.7 ± 2.7
	10.0	5		-	2.4 ± 0.6
	Ø	10		9.1	
ED_{50}(range) 0.25(0.2 - 0.4)					
ED_{90}(range) 2.5(1.8 - 4.1)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES) TABLE 85

COMPOUND NAME OR NUMBER ..CYCLOGUANIL..... PARASITE (SUB)SPECIES .P.yoelii ssp...

FORMULATION ..Tween.80/.H_2O. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.3	5		-	91.4 ± 15.6
	1.0	5		-	77.7 ± 8.3
QMS	3.0	5	1	-	1.1 ± 0.5
	10.0	5		-	0
	Ø	10		3.9	

ED_{50}(range)	1.0(0.4 - 1.9)
ED_{90}(range)	2.2(1.0 - 4.2)
Resistance factor I_{90}	

ED_{50}(range)	
ED_{90}(range)	
Resistance factor I_{90}	

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES) TABLE 86

COMPOUND NAME OR NUMBER MENOCTONE..... PARASITE (SUB)SPECIES P.berghei.....

FORMULATION Tween 80 / H_2O.. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.1	5		-	92.6 ± 5.8
	0.3	5		-	84.6 ± 7.2
MFY	1.0	5	1	-	46.0 ± 10.1
	3.0	5		-	1.8 ± 1.7
	10.0	5		-	0
	∅	10		9.9	
ED_{50}(range) 0.6(0.2 - 1.1)					
ED_{90}(range) 1.6(0.6 - 2.9)					
Resistance factor I_{90}					
	0.1	5		-	100 ± 4.9
	0.3	5		-	88.7 ± 6.0
KFY	1.0	5	1	-	62.3 ± 7.5
	3.0	5		-	3.2 ± 1.0
	10.0	5		-	0.6 ± 0.3
	∅	10		11.8	
ED_{50}(range) 0.9(0.5 - 1.5)					
ED_{90}(range) 2.5(1.5 - 4.2)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 87

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME

OR NUMBER MENOCTONE..... PARASITE (SUB)SPECIES P.berghei.....

FORMULATION Tween 80/H_2O. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	10.0	5		-	89.6 ± 3.3
	30.0	5		-	90.3 ± 3.1
MEN	100.0	5	1	-	70.4 ± 7.3
	300.0	5		-	55.3 ± 5.3
	Ø	10		21.0	

ED_{50}(range) 300(180 - 500)

ED_{90}(range) 3700(2200 - 6000)

Resistance factor I_{90}

	0.1	5		-	100
	0.3	5		-	89.4 ± 7.1
PFMA	1.0	5	1	-	50.9 ± 18.5
	3.0	5		-	6.8 ± 5.8
	10.0	5		-	0.03 ± 0.03
	Ø	10		5.9	

ED_{50}(range) 0.8(0.5 - 1.3)

ED_{90}(range) 2.0(1.5 - 3.4)

Resistance factor I_{90}

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES) TABLE 88

COMPOUND NAME OR NUMBER MENOCTONE..... PARASITE (SUB)SPECIES P. berghei.....

FORMULATION Tween 80 / H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0·1	5		-	96·9 ± 4·5
	0·3	5		-	82·5 ± 7·6
NAM	1·0	5	1	-	74·5 ± 5·1
	3·0	5		-	0·9 ± 0·3
	10·0	5		-	0·01 ± 0·01
	Ø	10		24·7	
ED_{50} (range) 0·7 (0·4 - 1·9)					
ED_{90} (range) 2·0 (1·0 - 5·5)					
Resistance factor I_{90}					
	0·1	5		-	87·8 ± 8·4
	0·3	5		-	71·5 ± 7·3
QM	1·0	5	1	-	58·6 ± 17·8
	3·0	5		-	19·5 ± 7·5
	10·0	5		-	0·02 ± 0·01
	Ø	10		19·4	
ED_{50} (range) 0·5 (0·2 - 2·3)					
ED_{90} (range) 2·9 (1·1 - 10·2)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES) TABLE 89

COMPOUND NAME OR NUMBER ..MENOCTONE..... PARASITE (SUB)SPECIES P.yoelii ssp..

FORMULATION Tween 80/H_2O... ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0·1	5		-	73·9 ± 4·7
	0·3	5		-	70·1 ± 7·7
SAM	1·0	5	1	-	57·7 ± 6·6
	3·0	5		-	16·1 ± 6·3
	10·0	5		-	0·3 ± 0·2
	Ø	10		17·3	
ED_{50}(range) 0·5(0·2 - 1·4)					
ED_{90}(range) 2·0(0·7 - 5·6)					
Resistance factor I_{90}					
	0·1	5		-	100 ± 6·6
	0·3	5		-	97·2 ± 10·9
MPS	1·0	5	1	-	77·4 ± 10·6
	3·0	5		-	1·3 ± 0·6
	10·0	5		-	0·03 ± 0·03
	Ø	10		6·4	
ED_{50}(range) 1·0(0·6 - 2·1)					
ED_{90}(range) 2·2(1·3 - 4·9)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
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London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES) TABLE 90

COMPOUND NAME OR NUMBER ..MENOCTONE..... PARASITE (SUB)SPECIES P.yoelii ssp....

FORMULATION ..Tween 80 / H_2O.. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.1	5		-	94.7 ± 9.3
	0.3	5		-	100 ± 9.3
QMS	1.0	5	1	-	78.6 ± 15.0
	3.0	5		-	4.6 ± 3.1
	10.0	5		-	0.05 ± 0.0
	∅	10		4.4	

ED_{50}(range)	1.3(0.8 - 2.3)
ED_{90}(range)	2.7(1.7 - 4.6)
Resistance factor I_{90}	

ED_{50}(range)	
ED_{90}(range)	
Resistance factor I_{90}	

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES)

TABLE 91

COMPOUND NAME OR NUMBER MENOCTONE..... PARASITE (SUB)SPECIES P.y.nigeriensis

FORMULATION Tween 80/H_2O.. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0·1	5		-	92·9 ± 5·8
	0·3	5		-	88·6 ± 7·1
NIG	1·0	5	1	-	72·4 ± 4·4
	3·0	6		-	5·7 ± 2·2
	10·0	5		-	1·0 ± 0·7
	ø	10		14·0	

ED_{50}(range)	0·9(0·3 - 1·8)
ED_{90}(range)	3·2(1·2 - 6·7)
Resistance factor I_{90}	

ED_{50}(range)	
ED_{90}(range)	
Resistance factor I_{90}	

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 92

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME

OR NUMBER ...FLOXACRINE..... PARASITE (SUB)SPECIES .P.berghei....

FORMULATION .Tween 80/H_2O. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.1	5		-	72.4 ± 11.3
	0.3	5		-	62.8 ± 9.4
MFY	1.0	5	1	-	1.0 ± 0.6
	3.0	5		-	0
	Ø	10		11.9	

ED_{50}(range)	0.2(0.1 - 0.4)
ED_{90}(range)	0.5(0.3 - 1.1)
Resistance factor I_{90}	

	0.1	5		-	96.6 ± 10.1
	0.3	5		-	55.2 ± 14.8
KFY	1.0	5	1	-	0.03 ± 0.01
	3.0	5		-	0
	Ø	10		14.7	

ED_{50}(range)	0.25(0.15 - 0.4)
ED_{90}(range)	0.45(0.3 - 0.6)
Resistance factor I_{90}	

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 93

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME

OR NUMBER ..FLOXACRINE..... PARASITE (SUB)SPECIES .P.yoelii.ssp..

FORMULATION .Tween.80/.H_2O. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.1	5		-	100
	0.3	5		-	62.4 ± 9.9
SAM	1.0	5	1	-	0.3 ± 0.1
	3.0	5		-	0.01 ± 0.01
	∅	10		25.1	

ED_{50} (range) 0.35 (0.3 - 0.4)

ED_{90} (range) 0.55 (0.4 - 0.5)

Resistance factor I_{90}

	0.1	5		-	92.5 ± 11.5
	0.3	5		-	51.9 ± 5.9
MPS	1.0	5	1	-	0.2 ± 0.1
	3.0	5		-	0
	∅	10		10.3	

ED_{50} (range) 0.25 (0.15 - 0.35)

ED_{90} (range) 0.5 (0.3 - 0.7)

Resistance factor I_{90}

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 94

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME

OR NUMBER ..FLOXACRINE..... PARASITE (SUB)SPECIES ..P.yoelii.ssp.

FORMULATION ..Tween 80/H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.1	5		-	80.3 ± 7.3
	0.3	5		-	62.4 ± 18.9
QMS	1.0	5	1	-	0.03 ± 0.03
	3.0	5		-	0
	Ø	10		6.6	

ED_{50}(range)	0.2(0.1 - 0.5)
ED_{90}(range)	0.4(0.25 - 0.9)
Resistance factor I_{90}	

ED_{50}(range)	
ED_{90}(range)	
Resistance factor I_{90}	

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 95

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME

OR NUMBER ..CLINDAMYCIN..... PARASITE (SUB)SPECIES ..P.berghei....

FORMULATION ..Tween.80/.H_2O. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X10C
	3.0	5		-	57.9 ± 4.2
	10.0	5		-	22.4 ± 4.2
MFY	30.0	5	1	-	3.5 ± 0.8
	100.0	5		-	1.3 ± 0.5
	Ø	10		11.9	
ED_{50}(range) 3.6(2.1-6.2)					
ED_{90}(range) 19.5(11.5-34.0)					
Resistance factor I_{90}					
	3.0	5		-	80.5 ± 15.2
	10.0	5		-	21.8 ± 7.4
KFY	30.0	5	1	-	4.4 ± 1.0
	100.0	5		-	2.9 ± 0.7
	Ø	10		14.7	
ED_{50}(range) 5.3(2.5-24.5)					
ED_{90}(range) 28.0(13.0-135)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
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London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES) TABLE 96

COMPOUND NAME OR NUMBER ..CLINDAMYCIN..... PARASITE (SUB)SPECIES ..P.berghei....

FORMULATION ..Tween 80/H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	3.0	5		-	75.0 ± 12.1
	10.0	5		-	46.9 ± 11.1
PFMA	30.0	5	1	-	5.5 ± 3.7
	100.0	5		-	0
	ø	10		16.4	

ED_{50}(range) 6.5(3.7 - 11.6)

ED_{90}(range) 16.5(9.3 - 29.0)

Resistance factor I_{90}

	3.0	5		-	75.4 ± 18.0
	10.0	5		-	49.9 ± 12.9
NAM	30.0	5	1	-	2.6 ± 1.2
	100.0	5		-	0.02 ± 0.02
	ø	10		9.3	

ED_{50}(range) 6.4(3.3 - 13.0)

ED_{90}(range) 18.5(9.7 - 37.0)

Resistance factor I_{90}

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES)

TABLE 97

COMPOUND NAME OR NUMBER ..CLINDAMYCIN..... PARASITE (SUB)SPECIES .P. berghei.....

FORMULATION .Tween 80/H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	3.0	5		-	46.4 ± 5.4
	10.0	5		-	28.2 ± 6.2
QM	30.0	5	1	-	1.3 ± 0.4
	100.0	5		-	0
	ø	10		20.7	

ED_{50}(range)	3.5(2.0 - 6.6)
ED_{90}(range)	13.8(8.0 - 26.5)
Resistance factor I_{90}	

ED_{50}(range)	
ED_{90}(range)	
Resistance factor I_{90}	

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 98

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME

OR NUMBER .CLINDAMYCIN..... PARASITE (SUB)SPECIES .P.yoelii ssp...

FORMULATION .Tween 80/H_2O.. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	3.0	5		-	65.2 ± 8.2
	10.0	5		-	30.6 ± 14.1
MPS	30.0	5	1	-	7.9 ± 1.1
	100.0	5		-	0.2 ± 0.2
	Ø	10		10.3	

ED_{50}(range) 5.6(3.5 - 8.2)

ED_{90}(range) 20.0(12.5 - 29.0)

Resistance factor I_{90}

	3.0	5		-	86.0 ± 4.8
	10.0	5		-	55.5 ± 13.1
SAM	30.0	5	1	-	15.3 ± 3.9
	100.0	5		-	0.4 ± 0.2
	Ø	10		25.1	

ED_{50}(range) 10.0(7.4 - 16.0)

ED_{90}(range) 32.0(21.0 - 52.0)

Resistance factor I_{90}

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES) TABLE 99

COMPOUND NAME OR NUMBER .CLINDAMYCIN..... PARASITE (SUB)SPECIES .P.yoelii.ssp..

FORMULATION .Tween.80./H_2O. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	3.0	5		-	88.8 ± 12.5
	10.0	5		-	66.4 ± 19.2
QMS	30.0	5	1	-	10.3 ± 4.1
	100.0	5		-	0.6 ± 0.3
	Ø	10		6.6	

ED_{50}(range)	10.0(5.2-22.5)
ED_{90}(range)	31.0(16.5-70.0)
Resistance factor I_{90}	

ED_{50}(range)	
ED_{90}(range)	
Resistance factor I_{90}	

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES)

TABLE 100

COMPOUND NAME OR NUMBER ..CLINDAMYCIN..... PARASITE (SUB)SPECIES P.y.nigeriensis..

FORMULATION .Tween.80/H_2O.. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	3.0	5		-	68.9 ± 15.1
	10.0	5		-	55.7 ± 11.1
NIG	30.0	5	1	-	5.8 ± 0.9
	100.0	5		-	1.4 ± 0.7
	Ø	10		25.2	

ED_{50}(range)	8.0(3.2 - 15.8)
ED_{90}(range)	28.5(11.8 - 57.0
Resistance factor I_{90}	

ED_{50}(range)	
ED_{90}(range)	
Resistance factor I_{90}	

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES)

TABLE 101

COMPOUND NAME OR NUMBER ..Doxycycline..... PARASITE (SUB)SPECIES ..P.berghei.....

FORMULATION ..Tween80/H_2O.. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	3.0	5		-	91.9 ± 6.3
	10.0	5		-	35.2 ± 3.9
N 1708	30.0	5	1	-	4.6 ± 2.1
	60.0	5		-	0.1 ± 0.1
	100.0	5		-	0
	Ø	10		19.2	
ED_{50}(range) 7.5(4.1 - 13.0)					
ED_{90}(range) 18.5(10.3 - 32.0)					
Resistance factor I_{90}					
	3.0	5		-	69.9 ± 14.5
	10.0	5		-	63.6 ± 11.6
MFY	30.0	5	1	-	6.8 ± 1.3
	60.0	5		-	3.5 ± 0.7
	100.0	5		-	2.1 ± 0.4
	Ø	10		8.6	
ED_{50}(range) 8.0(5.0 - 20.5)					
ED_{90}(range) 32.0(20.0 - 85.0)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES)

TABLE 102

COMPOUND NAME OR NUMBER ..Doxycycline..... PARASITE (SUB)SPECIES ..P. yoelii ssp..

FORMULATION ..Tween 80 / H_2O.. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	3.0	5		-	100 ± 3.4
	10.0	5		-	86.7 ± 6.5
NS	30.0	5	1	-	45.2 ± 15.1
	60.0	5		-	27.5 ± 13.3
	100.0	5		-	9.9 ± 5.4
	Ø	10		10.7	
ED_{50}(range) 28.5(17.5 - 48.0)					
ED_{90}(range) 98.0(60.0 - 170)					
Resistance factor I_{90}					
	3.0	5		-	83.1 ± 5.4
	10.0	5		-	63.7 ± 10.0
SPN	30.0	5	1	-	9.2 ± 4.0
	60.0	5		-	2.5 ± 1.0
	100.0	5		-	0
	Ø	10		12.9	
ED_{50}(range) 8.5(5.7 - 16.8)					
ED_{90}(range) 28.0(18.2 - 60.0)					
Resistance factor I_{90}					

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SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES)

TABLE 103

COMPOUND NAME OR NUMBER Doxycycline..... PARASITE (SUB)SPECIES P.y.nigeriensis

FORMULATION Tween 80 / H_2O. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	3.0	5		-	100 ± 1.6
	10.0	5		-	42.2 ± 10.0
NIG	30.0	5	1	-	7.0 ± 2.9
	60.0	5		-	3.3 ± 1.1
	100.0	5		-	2.3 ± 0.2
	Ø	10		25.4	

ED_{50}(range) 17.3(6.2-30.5)

ED_{90}(range) 37.5(16.0-67.0)

Resistance factor I_{90}

ED_{50}(range)

ED_{90}(range)

Resistance factor I_{90}

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APPENDIX 3

DRUG INTERACTION STUDIES

Figure 2.

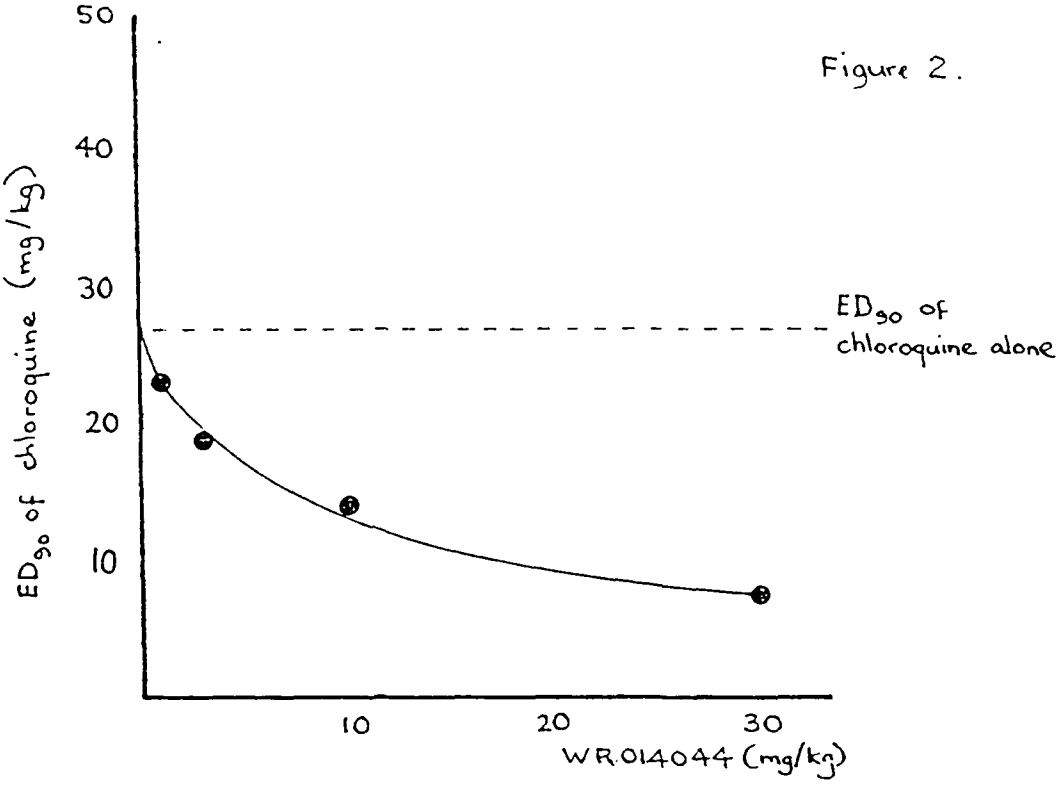
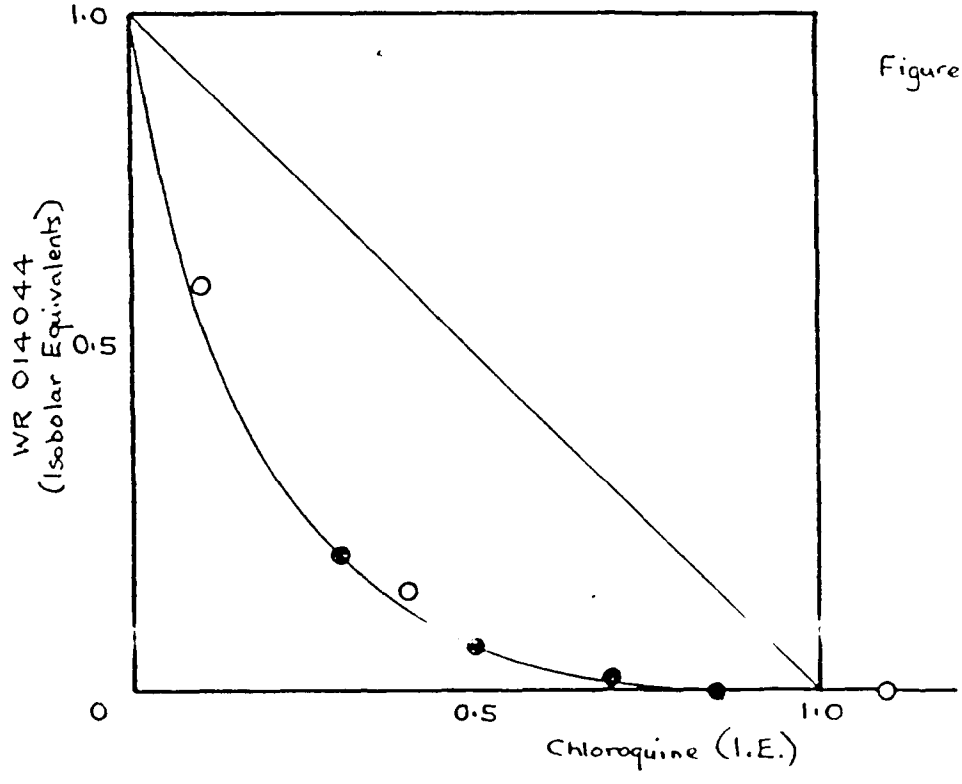


Figure 3.



Figures 2 and 3. The synergistic interaction of WR 014044 and chloroquine illustrated graphically by two alternative methods.

SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 104

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME WR 014044 BL 51831

OR NUMBER LON 2164 PARASITE (SUB)SPECIES P. yoelii ssp...

FORMULATION Tween 80/H_2O.. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	1.0	5		-	92.5 ± 7.1
	3.0	5		-	96.7 ± 1.9
NS	10.0	5	1	-	93.0 ± 4.3
	30.0	5		-	50.6 ± 9.3
	Ø	10		28.8	

ED_{50}(range)	30.0(3.8 - 110)
ED_{90}(range)	150(19.0 - 550)
Resistance factor I_{90}	

ED_{50}(range)	
ED_{90}(range)	
Resistance factor I_{90}	

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SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES)

TABLE 105

COMPOUND NAME OR NUMBER CHLOROQUINE..... PARASITE (SUB)SPECIES P.yoelii ssp..

FORMULATION Tween 80 / H_2O. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	3.0	5		-	60.5 ± 3.3
	10.0	5		-	18.5 ± 5.5
NS	30.0	5	1	-	12.5 ± 1.5
	60.0	5		-	6.4 ± 1.5
	∅	10		28.8	

ED_{50}(range)	3.2(1.5-5.8)
ED_{90}(range)	27.0(12.5-48.0)
Resistance factor I_{90}	

ED_{50}(range)	
ED_{90}(range)	
Resistance factor I_{90}	

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SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES)

TABLE 106

COMPOUND NAME OR NUMBER LON 2164 + CHLOROQUINE PARASITE (SUB)SPECIES P.yoelii ssp.

FORMULATION Tween 80/H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	1.0 + 3.0	5		-	81.0 ± 6.1
	3.0 + 3.0	5		-	79.4 ± 6.5
NS	10.0 + 3.0	5	1	-	57.2 ± 9.3
	30.0 + 3.0	5		-	32.7 ± 10.1
	Ø	10		28.8	

ED_{50}(range) 8.0(3.5 - 21.5)

ED_{90}(range) 88.0(36.0 - 235)

Resistance factor I_{90}

	1.0 + 10.0	5		-	9.7 ± 1.7
	3.0 + 10.0	5		-	9.0 ± 1.9
NS	10.0 + 10.0	5	1	-	7.9 ± 2.5
	30.0 + 10.0	5		-	1.5 ± 0.5
	Ø	10		28.8	

ED_{50}(range) < 0.1

ED_{90}(range) 2.3(0.7 - 10.1)

Resistance factor I_{90}

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES)

TABLE 107

COMPOUND NAME OR NUMBER LON 2164 + CHLOROQUINE PARASITE (SUB)SPECIES P.yoelii ssp.

FORMULATION Tween 80/H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X10(
	1.0 + 30.0	5		-	6.0 ± 1.9
	3.0 + 30.0	5		-	3.8 ± 1.5
NS	10.0 + 30.0	5	1	-	2.8 ± 1.0
	30.0 + 30.0	5		-	0.7 ± 0.2
	∅	10		28.8	
ED_{50}(range) < 0.1					
ED_{90}(range) 0.5(0.2 - 1.8)					
Resistance factor I_{90}					
	1.0 + 60.0	5		-	5.3 ± 1.1
	3.0 + 60.0	5		-	2.4 ± 0.8
NS	10.0 + 60.0	5	1	-	2.1 ± 1.1
	30.0 + 60.0	5		-	0.5 ± 0.2
	∅	10		28.8	
ED_{50}(range) < 0.1					
ED_{90}(range) 0.4 (0.2 - 1.2)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES)

TABLE 108

COMPOUND NAME OR NUMBER CHLOROQUINE + LON 2164. PARASITE (SUB)SPECIES P.yoelii ssp...

FORMULATION Tween 80 / H_2O... ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% x100
	3.0 + 1.0	5		-	81.0 ± 6.1
	10.0 + 1.0	5		-	9.7 ± 1.7
NS	30.0 + 1.0	5	1	-	6.0 ± 1.9
	60.0 + 1.0	5		-	5.3 ± 1.1
	∅	10		28.8	

ED_{50}(range)	6.7(2.6 - 13.5)
ED_{90}(range)	23.0(8.7 - 47.0)
Resistance factor I_{90}	

	3.0 + 3.0	5		-	79.4 ± 6.5
	10.0 + 3.0	5		-	9.0 ± 1.9
NS	30.0 + 3.0	5	1	-	3.8 ± 1.5
	60.0 + 3.0	5		-	2.4 ± 0.8
	∅	10		28.8	

ED_{50}(range)	6.0(2.7 - 11.3)
ED_{90}(range)	18.8(8.3 - 35.0)
Resistance factor I_{90}	

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES)

TABLE 109

COMPOUND NAME OR NUMBER CHLOROQUINE + LON 2164 PARASITE (SUB)SPECIES P. yoelii ssp....

FORMULATION Tween 80 / H_2O.. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X10
	3.0 + 10.0	5		-	57.2 ± 9.3
	10.0 + 10.0	5		-	7.9 ± 2.5
NS	30.0 + 10.0	5	1	-	2.8 ± 1.0
	60.0 + 10.0	5		-	2.1 ± 1.1
	∅	10		28.8	
ED_{50} (range) 3.5 (1.6 - 7.4)					
ED_{90} (range) 14.2 (6.6 - 31.0)					
Resistance factor I_{90}					
	3.0 + 30.0	5		-	32.7 ± 10.1
	10.0 + 30.0	5		-	1.5 ± 0.5
NS	30.0 + 30.0	5	1	-	0.7 ± 0.2
	60.0 + 30.0	5		-	0.5 ± 0.2
	∅	10		28.8	
ED_{50} (range) 1.7 (0.7 - 3.5)					
ED_{90} (range) 7.6 (2.9 - 15.5)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
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London School of Hygiene & Tropical Medicine

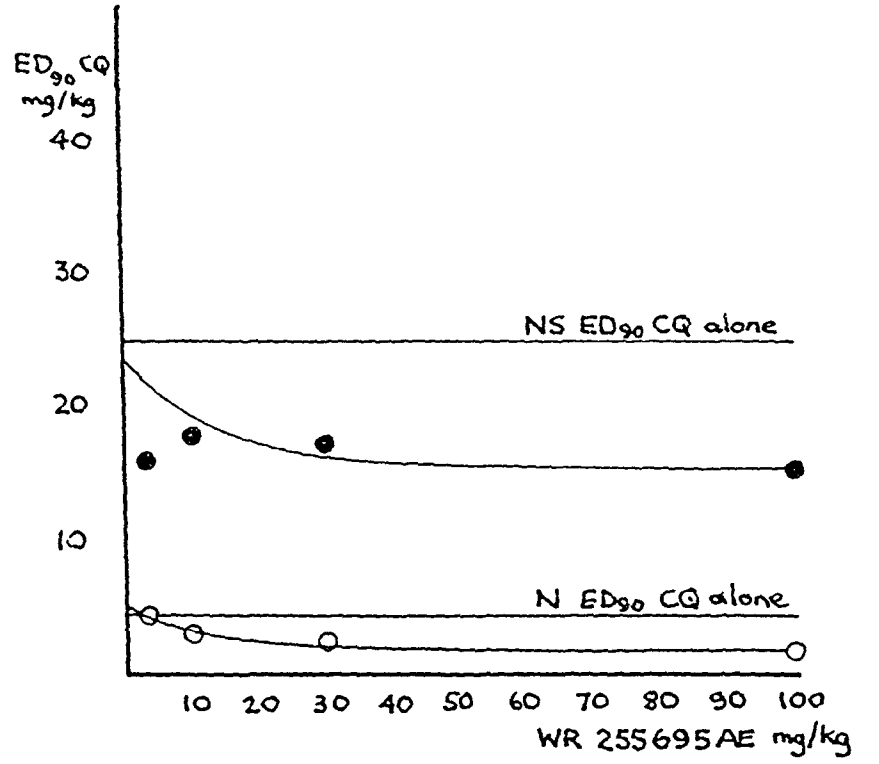

Figure 4. Interaction of WR255695AE and chloroquine.

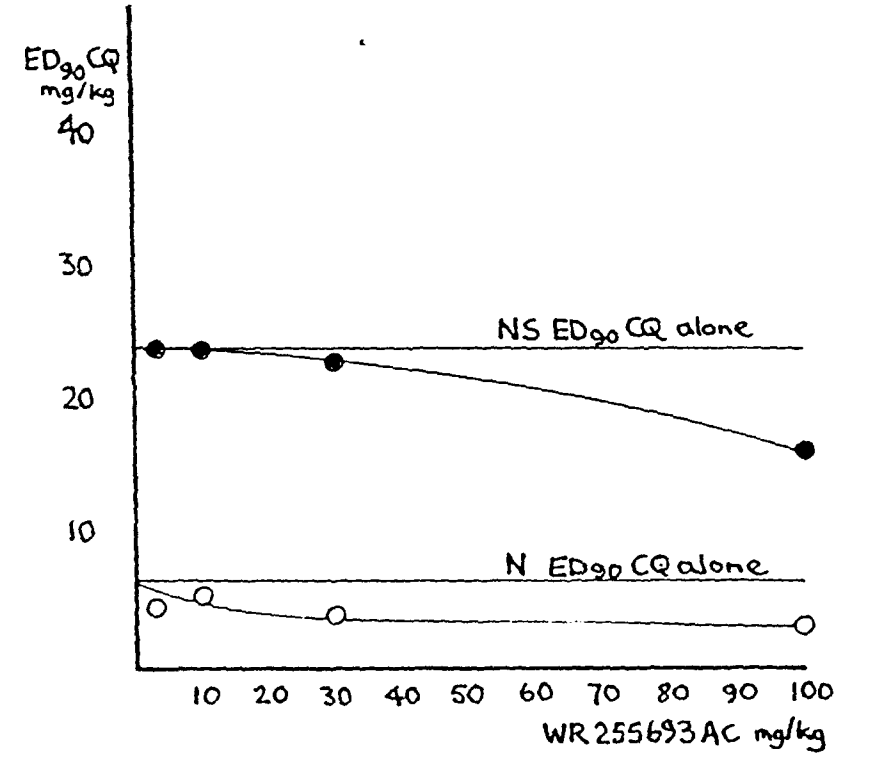

Figure 5. Interaction of WR255693AC and chloroquine.

SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES)

TABLE 110

COMPOUND NAME WR 255695AE(BL 48656)

OR NUMBER LON 2142 PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80/H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	3.0	5		—	92.9 ± 3.9
	10.0	5		—	100 ± 2.4
N	30.0	5	1	—	93.7 ± 3.2
	100.0	5		—	85.2 ± 2.3
	Ø	10		23.8	

ED_{50}(range)	>100
ED_{90}(range)	≫100
Resistance factor I_{90}	

ED_{50}(range)	
ED_{90}(range)	
Resistance factor I_{90}	

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES) TABLE III

COMPOUND NAME OR NUMBER CHLOROQUINE..... PARASITE (SUB)SPECIES P.berghei.....

FORMULATION Tween 80/H_2O. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.3	5		-	90.1 ± 4.7
	1.0	5		-	98.2 ± 4.4
N	3.0	5	1	-	51.4 ± 10.6
	10.0	5		-	0.08 ± 0.08
	Ø	10		23.8	

ED_{50}(range)	2.6 (1.9 – 3.3)
ED_{90}(range)	4.4 (3.3 – 5.6)
Resistance factor I_{90}	

ED_{50}(range)	
ED_{90}(range)	
Resistance factor I_{90}	

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES)

TABLE 112

COMPOUND NAME OR NUMBER LON 2142 + CHLOROQUINE PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80/H_2O. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X10
	3.0 + 0.3	5		-	91.0 ± 4.4
	10.0 + 0.3	5		-	83.4 ± 4.9
N	30.0 + 0.3	5	1	-	76.2 ± 2.2
	100.0 + 0.3	5		-	49.9 ± 6.6
	Ø	10		23.8	

ED_{50}(range)	90.0 (40.0 - 190)
ED_{90}(range)	≫ 100
Resistance factor I_{90}	

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X10
	3.0 + 1.0	5		-	82.2 ± 3.5
	10.0 + 1.0	5		-	78.2 ± 4.9
N	30.0 + 1.0	5	1	-	53.9 ± 6.1
	100.0 + 1.0	5		-	43.1 ± 4.4
	Ø	10		23.8	

ED_{50}(range)	50.0 (22.0 - 150)
ED_{90}(range)	≫ 100
Resistance factor I_{90}	

Principal Investigator: Professor W.Peters
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London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES)

TABLE 113

COMPOUND NAME OR NUMBER LON 2142 + CHLOROQUINE PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80/H_2O .. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X10(
	3.0 + 3.0	5		-	47.8 ± 11.1
	10.0 + 3.0	5		-	45.9 ± 1.8
N	30.0 + 3.0	5	1	-	31.3 ± 3.3
	100.0 + 3.0	5		-	32.2 ± 2.2
	Ø	10		23.8	

ED_{50}(range) 3.0(1.0 - 9.0)

ED_{90}(range) > 100

Resistance factor I_{90}

	3.0 + 10.0	5		-	0.3 ± 0.2
	10.0 + 10.0	5		-	0
N	30.0 + 10.0	5	1	-	0
	100.0 + 10.0	5		-	0
	Ø	10		23.8	

ED_{50}(range) < 3.0

ED_{90}(range) < 3.0

Resistance factor I_{90}

Principal Investigator: Professor W.Peters
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London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES)

TABLE 114

COMPOUND NAME OR NUMBER Chloroquine + LON 2142 PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80/H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.3 + 3.0	5		-	91.0 ± 4.4
	1.0 + 3.0	5		-	82.2 ± 3.5
N	3.0 + 3.0	5	1	-	47.8 ± 11.1
	10.0 + 3.0	5		-	0.3 ± 0.2
	Ø	10		23.8	

ED_{50}(range) 1.5(0.7 – 3.5)

ED_{90}(range) 4.5(2.1 – 10.0)

Resistance factor I_{90}

	0.3 + 10.0	5		-	83.4 ± 4.9
	1.0 + 10.0	5		-	78.2 ± 4.9
N	3.0 + 10.0	5	1	-	45.9 ± 1.8
	10.0 + 10.0	5		-	0
	Ø	10		23.8	

ED_{50}(range) 1.3(0.4 – 2.9)

ED_{90}(range) 2.6(0.9 – 5.6)

Resistance factor I_{90}

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES)

TABLE 115

COMPOUND NAME OR NUMBER CHLOROQUINE + LON 2142 PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80/H_2O .. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.3 + 30.0	5		-	76.2 ± 2.2
	1.0 + 30.0	5		-	53.9 ± 6.1
N	3.0 + 30.0	5	1	-	31.3 ± 3.3
	10.0 + 30.0	5		-	0
	Ø	10		23.8	

ED_{50}(range)	1.0(0.6-2.3)
ED_{90}(range)	2.3(1.2-5.0)
Resistance factor I_{90}	

	0.3 + 100.0	5		-	49.9 ± 6.6
	1.0 + 100.0	5		-	43.1 ± 4.4
N	3.0 + 100.0	5	1	-	32.2 ± 2.2
	10.0 + 100.0	5		-	0
	Ø	10		23.8	

ED_{50}(range)	0.8(0.3-2.2)
ED_{90}(range)	1.9(0.6-5.1)
Resistance factor I_{90}	

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES)

TABLE 116

COMPOUND NAME WR 255695 AE (BL 48656)

OR NUMBER LON 2142 PARASITE (SUB)SPECIES P. yoelii ssp...

FORMULATION Tween 80/H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	3.0	5		-	98.6 ± 1.4
	10.0	5		-	92.0 ± 4.8
NS	30.0	5	1	-	94.1 ± 2.5
	100.0	5		-	94.1 ± 2.3
	Ø	10		28.1	

ED_{50}(range)	> 100
ED_{90}(range)	≫ 100
Resistance factor I_{90}	

ED_{50}(range)	
ED_{90}(range)	
Resistance factor I_{90}	

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES)

TABLE 117

COMPOUND NAME

OR NUMBER .CHLOROQUINE..... PARASITE (SUB)SPECIES .P. yoelii ssp..

FORMULATION .Tween 80./. H_2O. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	3.0	5		-	90.1 ± 3.3
	10.0	5		-	41.0 ± 1.9
NS	30.0	5	1	-	3.5 ± 1.3
	60.0	5		-	1.1 ± 0.8
	∅	10		28.1	

ED_{50}(range)	8.3(4.9 - 16.5)
ED_{90}(range)	25.0(15.0 - 50.0)
Resistance factor I_{90}	

ED_{50}(range)	
ED_{90}(range)	
Resistance factor I_{90}	

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES)

TABLE 118

COMPOUND NAME OR NUMBER LON 2142 + CHLOROQUINE PARASITE (SUB)SPECIES P.yoelii ssp.

FORMULATION Tween 80/H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	3.0 + 1.0	5		-	88.9 ± 3.4
	10.0 + 1.0	5		-	92.3 ± 2.0
NS	30.0 + 1.0	5	-	-	91.8 ± 2.5
	100.0 + 1.0	5		-	89.2 ± 2.5
	∅	10		28.1	
ED_{50}(range) > 100					
ED_{90}(range) ≫ 100					
Resistance factor I_{90}					
	3.0 + 3.0	5		-	92.4 ± 3.3
	10.0 + 3.0	5		-	89.1 ± 2.0
NS	30.0 + 3.0	5	1	-	92.7 ± 2.8
	100.0 + 3.0	5		-	87.9 ± 3.9
	∅	10		28.1	
ED_{50}(range) > 100					
ED_{90}(range) ≫ 100					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES)

TABLE 119

COMPOUND NAME OR NUMBER LON 2142 + CHLOROQUINE PARASITE (SUB)SPECIES P.yoelii ssp..

FORMULATION Tween 80/H_2O.. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	3.0 + 10.0	5		-	2.6 ± 1.4
	10.0 + 10.0	5		-	4.2 ± 1.1
NS	30.0 + 10.0	5	1	-	4.0 ± 1.2
	100.0 + 10.0	5		-	2.1 ± 0.5
	∅	10		28.1	
ED_{50}(range) < 3.0					
ED_{90}(range) < 3.0					
Resistance factor I_{90}					
	3.0 + 30.0	5		-	1.8 ± 1.0
	10.0 + 30.0	5		-	1.4 ± 0.3
NS	30.0 + 30.0	5	1	-	1.7 ± 0.3
	100.0 + 30.0	5		-	1.4 ± 0.7
	∅	10		28.1	
ED_{50}(range) < 3.0					
ED_{90}(range) < 3.0					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES)

TABLE 120

COMPOUND NAME OR NUMBER LON 2142 + CHLOROQUINE PARASITE (SUB)SPECIES P. yoelii ssp.

FORMULATION Tween 80/H_2O. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	3.0 + 60.0	5		-	0.6 ± 0.2
	10.0 + 60.0	5		-	1.4 ± 0.2
NS	30.0 + 60.0	5	1	-	1.4 ± 0.6
	100.0 + 60.0	5		-	1.4 ± 0.6
	Ø	10		28.1	

ED_{50}(range) < 3.0	
ED_{90}(range) < 3.0	
Resistance factor I_{90}	

ED_{50}(range)	
ED_{90}(range)	
Resistance factor I_{90}	

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SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES) TABLE 121

COMPOUND NAME OR NUMBER CHLOROQUINE + LON 2142 PARASITE (SUB)SPECIES P. yoelii ssp...

FORMULATION Tween 80/H_2O.. ROUTE OF ADMINISTRATION : SC/~~IV/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	1.0 + 3.0	5		-	88.9 ± 3.4
	3.0 + 3.0	5		-	92.4 ± 3.3
NS	10.0 + 3.0	5	1	-	2.6 ± 1.4
	30.0 + 3.0	5		-	1.8 ± 1.0
	60.0 + 3.0	5		-	0.6 ± 0.2
	Ø	10		28.1	
ED_{50}(range) 8.0(2.2-21.0)					
ED_{90}(range) 16.0(5.0-48.0)					
Resistance factor I_{90}					
	1.0 + 10.0	5		-	92.3 ± 2.0
	3.0 + 10.0	5		-	89.1 ± 2.0
NS	10.0 + 10.0	5	1	-	4.2 ± 1.1
	30.0 + 10.0	5		-	1.4 ± 0.3
	60.0 + 10.0	5		-	1.4 ± 0.2
	Ø	10		28.1	
ED_{50}(range) 5.0(1.5-11.0)					
ED_{90}(range) 17.8(5.2-40.0)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES)

TABLE 122

COMPOUND NAME OR NUMBER CHLOROQUINE + LON 242 PARASITE (SUB)SPECIES P. yoelii ssp...

FORMULATION Tween 80/H_2O.. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	1.0 + 30.0	5		-	91.8 ± 2.5
	3.0 + 30.0	5		-	92.7 ± 2.8
NS	10.0 + 30.0	5	1	-	4.0 ± 1.2
	30.0 + 30.0	5		-	1.7 ± 0.3
	100.0 + 30.0	5		-	1.4 ± 0.6
	∅	10		28.1	
ED_{50}(range) 5.0 (1.6 - 14.5)					
ED_{90}(range) 17.5 (5.3 - 50.0)					
Resistance factor I_{90}					
	1.0 + 60.0	5		-	89.2 ± 2.5
	3.0 + 60.0	5		-	87.9 ± 3.9
NS	10.0 + 60.0	5	1	-	2.1 ± 0.5
	30.0 + 60.0	5		-	1.4 ± 0.7
	100.0 + 60.0	5		-	1.4 ± 0.6
	∅	10		28.1	
ED_{50}(range) 6.4 (2.2 - 24.0)					
ED_{90}(range) 15.5 (5.3 - 56.0)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES)

TABLE 123

COMPOUND NAME WR 255693 Ac (BL48657)

OR NUMBER LON 2143 PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80/H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) >100 MG/KG X 4.

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	3.0	5		-	98.4 ± 2.5
	10.0	5		-	82.2 ± 4.6
N	30.0	5	1	-	75.1 ± 7.9
	100.0	5		-	59.2 ± 5.9
	Ø	10		21.8	

ED_{50}(range)	80.0(30.0 - 160)
ED_{90}(range)	540(210 - >1000)
Resistance factor I_{90}	

ED_{50}(range)	
ED_{90}(range)	
Resistance factor I_{90}	

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES)

TABLE 124

COMPOUND NAME OR NUMBER CHLOROQUINE..... PARASITE (SUB)SPECIES .P.berghei.....

FORMULATION .Tween 80/H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.3	5		-	90.4 ± 3.0
	1.0	5		-	91.7 ± 2.8
N	3.0	5	1	-	80.6 ± 3.0
	10.0	5		-	0.7 ± 0.4
	∅	10		21.8	

ED_{50}(range)	3.1 (1.9 – 5.2)
ED_{90}(range)	6.5 (3.9 – 11.0)
Resistance factor I_{90}	

ED_{50}(range)	
ED_{90}(range)	
Resistance factor I_{90}	

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES)

TABLE 125

COMPOUND NAME OR NUMBER LON 2143 + CHLOROQUINE PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80/H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	3.0 + 0.3	5		-	97.6 ± 2.7
	10.0 + 0.3	5		-	89.7 ± 4.3
N	30.0 + 0.3	5	1	-	90.7 ± 2.8
	100.0 + 0.3	5		-	83.7 ± 5.0
	Ø	10		21.8	
ED_{50}(range)					
ED_{90}(range) NA 100					
Resistance factor I_{90}					
	3.0 + 1.0	5		-	88.6 ± 6.0
	10.0 + 1.0	5		-	90.2 ± 3.5
N	30.0 + 1.0	5	1	-	86.4 ± 1.4
	100.0 + 1.0	5		-	78.0 ± 6.2
	Ø	10		21.8	
ED_{50}(range)					
ED_{90}(range) > 100					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
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London School of Hygiene & Tropical Medicine

SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES)

TABLE 126

COMPOUND NAME OR NUMBER LON 2143 + CHLOROQUINE PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80/H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% x100
	3.0 + 3.0	5		-	34.8 ± 3.6
	10.0 + 3.0	5		-	56.8 ± 16.8
N	30.0 + 3.0	5	1	-	36.6 ± 15.6
	100.0 + 3.0	5		-	34.8 ± 9.8
	∅	10		21.8	
ED_{50}(range)					
ED_{90}(range) >100					
Resistance factor I_{90}					
	3.0 + 10.0	5		-	0.2 ± 0.2
	10.0 + 10.0	5		-	0.4 ± 0.3
N	30.0 + 10.0	5	1	-	0.09 ± 0.09
	100.0 + 10.0	5		-	0
	∅	10		21.8	
ED_{50}(range) < 100					
ED_{90}(range) << 100					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
Department of Medical Protozoology
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SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES) TABLE 127

COMPOUND NAME OR NUMBER CHLOROQUINE + LDN.2143 PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween.80./H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.3 + 3.0	5		-	97.6 ± 2.7
	1.0 + 3.0	5		-	88.6 ± 6.0
N	3.0 + 3.0	5	1	-	34.8 ± 3.6
	10.0 + 3.0	5		-	0.2 ± 0.2
	Ø	10		21.8	

ED_{50}(range)	1.8(0.6-3.2)
ED_{90}(range)	4.6(1.5-8.5)
Resistance factor I_{90}	

	0.3 + 1.0	5		-	89.7 ± 4.3
	1.0 + 1'0	5		-	90.2 ± 3.5
N	3.0 + 1.0	5	1	-	56.8 ± 16.8
	10.0 + 1.0	5		-	0.4 ± 0.3
	Ø	10		21.8	

ED_{50}(range)	2.6(1.6-4.2)
ED_{90}(range)	5.4(3.3-9.0)
Resistance factor I_{90}	

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SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES)

TABLE 128

COMPOUND NAME OR NUMBER CHLOROQUINE + LON 2143 PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80/H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.3 + 30.0	5		-	90.7 ± 2.8
	1.0 + 30.0	5		-	86.4 ± 1.4
N	3.0 + 30.0	5	1	-	36.6 ± 15.6
	10.0 + 30.0	5		-	0.09 ± 0.09
	Ø	10		21.8	

ED_{50} (range) 2.0 (1.4 - 3.1)

ED_{90} (range) 4.0 (2.7 - 6.0)

Resistance factor I_{90}

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.3 + 100.0	5		-	83.7 ± 5.0
	1.0 + 100.0	5		-	78.0 ± 6.2
N	3.0 + 100.0	5	1	-	34.2 ± 9.8
	10.0 + 100.0	5		-	0
	Ø	10		21.8	

ED_{50} (range) 1.7 (1.3 - 2.7)

ED_{90} (range) 3.1 (2.3 - 5.0)

Resistance factor I_{90}

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 129

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME WR 255693 AC (BL 48657)

OR NUMBER LON 2143 PARASITE (SUB)SPECIES P. yoelli ssp.

FORMULATION Tween 80/H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ≥100 MG/KG X 4

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	3.0	5		-	100 ± 0.6
	10.0	5		-	96.5 ± 1.2
NS	30.0	5	1	-	94.2 ± 0.5
	100.0	5		-	88.1 ± 6.3
	Ø	10		27.8	

ED_{50}(range)	>100
ED_{90}(range)	>>100
Resistance factor I_{90}	

ED_{50}(range)	
ED_{90}(range)	
Resistance factor I_{90}	

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SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES)

TABLE 130

COMPOUND NAME OR NUMBER CHLOROQUINE..... PARASITE (SUB)SPECIES ..P.yoelii ssp..

FORMULATION Tween 80/H_2O.. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	3.0	5		-	85.8 ± 5.5
	10.0	5		-	39.0 ± 0.6
NS	30.0	5	1	-	2.3 ± 0.8
	60.0	5		-	1.2 ± 0.3
	Ø	10		27.8	

ED_{50}(range)	7.8(4.3 - 14.5)
ED_{90}(range)	24.0(13.0 - 42.0)
Resistance factor I_{90}	

ED_{50}(range)	
ED_{90}(range)	
Resistance factor I_{90}	

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SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES)

TABLE 131

COMPOUND NAME OR NUMBER LON 2143 + CHLOROQUINE PARASITE (SUB)SPECIES P. yoelii ssp.

FORMULATION Tween 80 / H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	3.0 + 1.0	5		–	87.9 ± 7.5
	10.0 + 1.0	5		–	93.9 ± 2.5
NS	30.0 + 1.0	5	1	–	91.9 ± 1.1
	100.0 + 1.0	5		–	100 ± 1.2
	Ø	10		27.8	

ED_{50}(range)	> 100
ED_{90}(range)	≫ 100
Resistance factor I_{90}	

	3.0 + 3.0	5		–	83.5 ± 2.3
	10.0 + 3.0	5		–	75.8 ± 6.6
NS	30.0 + 3.0	5	1	–	72.5 ± 5.3
	100.0 + 3.0	5		–	64.6 ± 10.9
	Ø	10		27.8	

ED_{50}(range)	> 100
ED_{90}(range)	> 100
Resistance factor I_{90}	

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES)

TABLE 132

COMPOUND NAME OR NUMBER LON 2143 + CHLOROQUINE PARASITE (SUB)SPECIES P. yoelii ssp...

FORMULATION Tween80 / H_2O. ROUTE OF ADMINISTRATION : SC/IP/PO/IV

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	3.0 + 10.0	5		-	40.4 ± 1.8
	10.0 + 10.0	5		-	38.2 ± 0.2
NS	30.0 + 10.0	5	1	-	41.7 ± 1.4
	100.0 + 10.0	5		-	37.7 ± 0.5
	∅	10		27.8	

ED_{50}(range)	
ED_{90}(range)	>100
Resistance factor I_{90}	

	3.0 + 30.0	5		-	2.3 ± 1.0
	10.0 + 30.0	5		-	2.7 ± 1.0
NS	30.0 + 30.0	5	1	-	1.9 ± 1.0
	100.0 + 30.0	5		-	1.8 ± 0.7
	∅	10		27.8	

ED_{50}(range)	<3.0
ED_{90}(range)	<3.0
Resistance factor I_{90}	

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SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES)

TABLE 133

COMPOUND NAME OR NUMBER LON 2143 + CHLOROQUINE PARASITE (SUB)SPECIES P.yoelii ssp...

FORMULATION Tween 80/H_2O.. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	3.0 + 60.0	5		-	1.9 ± 0.6
	10.0 + 60.0	5		-	1.2 ± 0.5
NS	30.0 + 60.0	5	1	-	1.8 ± 0.6
	100.0 + 60.0	5		-	0.6 ± 0.3
	∅	10		27.8	

ED_{50}(range) < 3.0	
ED_{90}(range) < 3.0	
Resistance factor I_{90}	

ED_{50}(range)	
ED_{90}(range)	
Resistance factor I_{90}	

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 134

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME

OR NUMBER CHLOROQUINE + LON 2143 PARASITE (SUB)SPECIES P.yoelii ssp....

FORMULATION Tween 80/H_2O... ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	1.0 + 3.0	5		-	87.9 ± 7.5
	3.0 + 3.0	5		-	83.5 ± 2.3
NS	10.0 + 3.0	5	1	-	40.4 ± 1.8
	30.0 + 3.0	5		-	2.3 ± 1.0
	60.0 + 3.0	5		-	1.9 ± 0.6
	Ø	10		27.8	
ED_{50}(range) 7.2(2.2 - 15.5)					
ED_{90}(range) 24.0(7.0 - 50.0)					
Resistance factor I_{90}					
	1.0 + 10.0	5		-	93.9 ± 2.5
	3.0 + 10.0	5		-	75.8 ± 6.6
NS	10.0 + 10.0	5	1	-	38.2 ± 0.2
	30.0 + 10.0	5		-	2.7 ± 1.0
	60.0 + 10.0	5		-	1.2 ± 0.5
	Ø	10		27.8	
ED_{50}(range) 6.2(3.0 - 10.2)					
ED_{90}(range) 24.0(11.8 - 40.0)					
Resistance factor I_{90}					

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SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES)

TABLE 135

COMPOUND NAME OR NUMBER Chloroquine + LON 2143. PARASITE (SUB)SPECIES P.yoelii ssp....

FORMULATION Tween 80/H_2O.. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	1.0 + 30.0	5		-	91.9 ± 1.1
	3.0 + 30.0	5		-	72.5 ± 5.3
NS	10.0 + 30.0	5	1	-	41.7 ± 1.4
	30.0 + 30.0	5		-	1.9 ± 1.0
	60.0 + 30.0	5		-	1.8 ± 0.6
	Ø	10		27.8	
ED_{50}(range) 5.1 (1.9 - 8.8)					
ED_{90}(range) 23.0 (8.0 - 39.0)					
Resistance factor I_{90}					
	1.0 + 100.0	5		-	100 ± 1.2
	3.0 + 100.0	5		-	64.6 ± 10.9
NS	10.0 + 100.0	5	1	-	37.7 ± 0.5
	30.0 + 100.0	5		-	1.8 ± 0.7
	60.0 + 100.0	5		-	0.6 ± 0.3
	Ø	10		27.8	
ED_{50}(range) 7.3 (3.0 - 22.0)					
ED_{90}(range) 16.5 (6.6 - 48.0)					
Resistance factor I_{90}					

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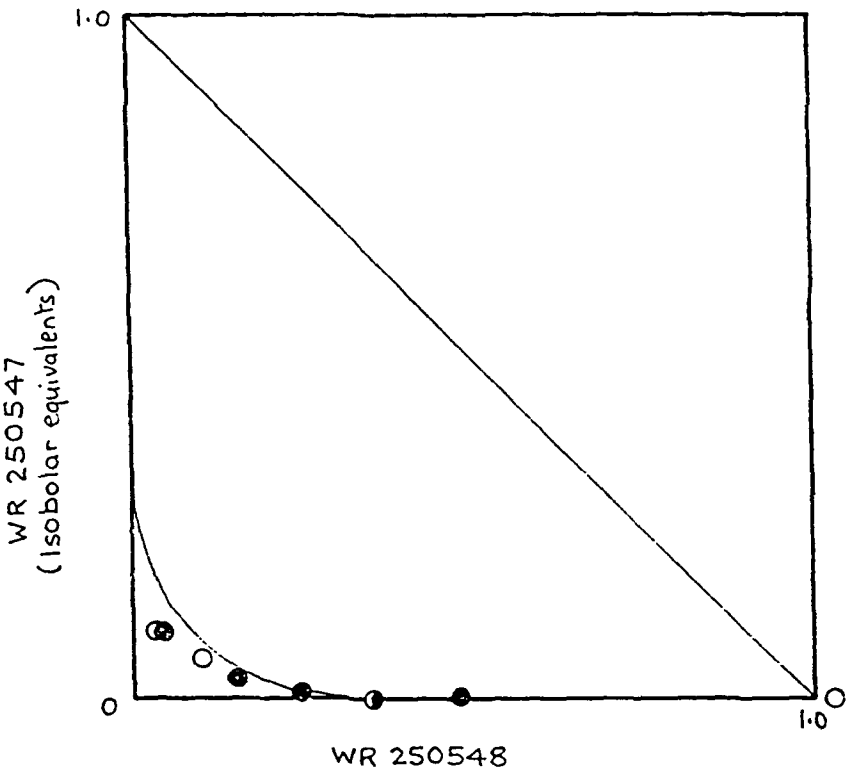

Figure 6. Isobologram illustrating synergism between the two isomers of the floxacrine analogue WR 243251.

SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES)

TABLE 136

COMPOUND NAME WR 250547 (BL 29759)

OR NUMBER LON 2160 PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween80/H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X10C
	0.1	5		-	94.0 ± 2.9
	0.3	5		-	84.9 ± 1.2
N	1.0	5	1	-	87.8 ± 2.3
	3.0	5		-	87.8 ± 1.6
	10.0	5		-	62.6 ± 7.2
	Ø	10		21.6	

ED_{50}(range)	15.0(11.3-18.3)
ED_{90}(range)	90.0(69.0-110)
Resistance factor I_{90}	

ED_{50}(range)	
ED_{90}(range)	
Resistance factor I_{90}	

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SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 137

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME WR 250548 (BL 34170)

OR NUMBER LON 2161 PARASITE (SUB)SPECIES P.berghei

FORMULATION Tween 80/H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.1	5		-	75.9 ± 6.9
	0.3	5		-	65.2 ± 5.4
N	1.0	5	1	-	35.4 ± 8.8
	3.0	5		-	10.1 ± 4.1
	10.0	5		-	2.2 ± 0.7
	∅	10		21.6	

ED_{50}(range)	0.4 (0.2 - 0.8)
ED_{90}(range)	2.9 (1.5 - 5.5)
Resistance factor I_{90}	

ED_{50}(range)	
ED_{90}(range)	
Resistance factor I_{90}	

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SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES)

TABLE 138

COMPOUND NAME OR NUMBER LON.2160.+.LON.2161. PARASITE (SUB)SPECIES .P.berghei....

FORMULATION .Tween.80/.H_2O. ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.1 + 0.1	5		–	90.9 ± 2.1
	0.3 + 0.1	5		–	84.0 ± 2.0
N	1.0 + 0.1	5	1	–	77.2 ± 5.7
	3.0 + 0.1	5		–	44.0 ± 15.0
	10.0 + 0.1	5		–	9.8 ± 4.2
	Ø	10		21.6	
ED_{50}(range) 1.3(0.6–4.3)					
ED_{90}(range) 9.5(4.0–30.0)					
Resistance factor I_{90}					
	0.1 + 0.3	5		–	64.0 ± 6.7
	0.3 + 0.3	5		–	53.1 ± 4.5
N	1.0 + 0.3	5	1	–	47.2 ± 10.8
	3.0 + 0.3	5		–	19.8 ± 12.0
	10.0 + 0.3	5		–	6.0 ± 1.6
	Ø	10		21.6	
ED_{50}(range) 0.4(0.1 – 1.4)					
ED_{90}(range) 5.5(2.0 – 20.5)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 139

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME OR NUMBER LON 2160 + LON 2161 PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80/H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.1 + 1.0	5		-	39.6 ± 14.6
	0.3 + 1.0	5		-	11.4 ± 1.2
N	1.0 + 1.0	5	1	-	7.0 ± 2.2
	3.0 + 1.0	5		-	2.5 ± 1.0
	10.0 + 1.0	5		-	1.6 ± 0.6
	∅	10		21.6	
ED_{50}(range) 0.05 (0.02 – 0.18)					
ED_{90}(range) 0.7 (0.3 – 2.2)					
Resistance factor I_{90}					
	0.1 + 3.0	5		-	4.8 ± 0.7
	0.3 + 3.0	5		-	2.5 ± 0.6
N	1.0 + 3.0	5	1	-	0.2 ± 0.2
	3.0 + 3.0	5		-	0
	10.0 + 3.0	5		-	0
	∅	10		21.6	
ED_{50}(range) 0.01 (<0.01 – 0.02)					
ED_{90}(range) 0.07 (0.05 – 0.12)					
Resistance factor I_{90}					

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES)

TABLE 140

COMPOUND NAME OR NUMBER LON 2160 + LON 2161 PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80/H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.1 + 10.0	5		-	0
	0.3 + 10.0	5		-	0
N	1.0 + 10.0	5	1	-	0
	3.0 + 10.0	5		-	0
	10.0 + 10.0	5		-	0
	Ø	10		21.6	

ED_{50}(range)	
ED_{90}(range)	
Resistance factor I_{90}	

ED_{50}(range)	
ED_{90}(range)	
Resistance factor I_{90}	

Principal Investigator: Professor W.Peters
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SUMMARY OF ANTIMALARIAL DRUG TESTS TABLE 141

(BLOOD SCHIZONTOCIDES)

COMPOUND NAME

OR NUMBER LON 2161 + LON 2160 PARASITE (SUB)SPECIES P. berghei....

FORMULATION Tween 80/H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.1 + 0.1	5		-	90.9 ± 2.1
	0.3 + 0.1	5		-	64.0 ± 6.7
N	1.0 + 0.1	5	1	-	39.6 ± 14.6
	3.0 + 0.1	5		-	4.8 ± 0.7
	10.0 + 0.1	5		-	0
	∅	10		21.6	
ED_{50}(range) 0.5(0.2 - 1.1)					
ED_{90}(range) 1.4(0.7 - 2.8)					
Resistance factor I_{90}					
	0.1 + 0.3	5		-	84.0 ± 2.0
	0.3 + 0.3	5		-	53.1 ± 4.5
N	1.0 + 0.3	5	1	-	11.4 ± 1.2
	3.0 + 0.3	5		-	2.5 ± 0.6
	10.0 + 0.3	5		-	0
	∅	10		21.6	
ED_{50}(range) 0.3(0.2 - 0.5)					
ED_{90}(range) 1.0(0.7 - 1.7)					
Resistance factor I_{90}					

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SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES)

TABLE 142

COMPOUND NAME OR NUMBER LON 2161 + LON 2160 PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80 / H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg DO-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.1 + 1.0	5		-	77.2 ± 5.7
	0.3 + 1.0	5		-	47.2 ± 10.8
N	1.0 + 1.0	5	1	-	7.0 ± 2.2
	3.0 + 1.0	5		-	0.2 ± 0.2
	10.0 + 1.0	5		-	0
	Ø	10		21.6	

ED_{50} (range) 0.2 (0.15 - 0.35)

ED_{90} (range) 0.7 (0.5 - 1.0)

Resistance factor I_{90}

	0.1 + 3.0	5		-	44.0 ± 15.0
	0.3 + 3.0	5		-	19.8 ± 12.0
N	1.0 + 3.0	5	1	-	2.5 ± 1.0
	3.0 + 3.0	5		-	0
	10.0 + 3.0	5		-	0
	Ø	10		21.6	

ED_{50} (range) 0.09 (0.05 - 0.17)

ED_{90} (range) 0.42 (0.23 - 0.8)

Resistance factor I_{90}

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SUMMARY OF ANTIMALARIAL DRUG TESTS (BLOOD SCHIZONTOCIDES)

TABLE 143

COMPOUND NAME OR NUMBER LON 2161 + LON 2160. PARASITE (SUB)SPECIES P. berghei

FORMULATION Tween 80/H_2O ROUTE OF ADMINISTRATION : SC/~~IP/PO/IV~~

MAXIMUM TOLERATED DOSE (MTD) ..... MG/KG X ...

Strain	Daily dose mg/kg D0-D+3	No. of mice	No. of experiments	Mean control parasite rate %	Treated PR% / Control PR% X100
	0.1 + 10.0	5		-	9.8 ± 4.2
	0.3 + 10.0	5		-	6.0 ± 1.6
N	1.0 + 10.0	5	1	-	1.6 ± 0.6
	3.0 + 10.0	5		-	0
	10.0 + 10.0	5		-	0
	Ø	10		21.6	

ED_{50}(range)	0.01 (<0.01 - 0.02)
ED_{90}(range)	0.12 (0.05 - 0.24)
Resistance factor I_{90}	

ED_{50}(range)	
ED_{90}(range)	
Resistance factor I_{90}	

Principal Investigator: Professor W.Peters
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